JONATHAN BORAK & COMPANY, INC
Specialists in Occupational & Environmental Health

October 8, 2003

Mr. Marvin W. Nichols, Jr.
Director, Office of Standards, Regulations & Variances
MSHA
1100 Wilson Blvd.
Arlington, VA 22209-3939

Dear Mr. Nichols:

Enclosed with this letter are my updated comments on the Proposed Final Rule for Diesel Particulate Matter Exposure of Underground Metal and Nonmetal Miners (*Fed Reg* 68:48668 *et seq*., August 14, 2003). I have also included copies of my three previous sets of comments and my current CV.

In preparing these comments, I considered whether recently published scientific reports have altered the opinions contained in my earlier comments. My updated review of the scientific literature confirms my prior opinion: the MSHA PELs are not scientifically supported.

Thank you for your considerations

Yours truly,

Jonathan Borak, MD, DABT, FACP, FACOEM, FRCPC

cc: Hon. David Lauriski
Mr. Henry Chajet

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Diesel Particulate Matter Exposure of Underground Metal and Nonmetal Miners: Final Rule

Federal Register 66:5706-5910, 2001

Updated Comments of Jonathan Borak, MD

October 8, 2003

Over the past four years, I have submitted three sets of comments to MSHA concerning its proposed rules for Diesel Particulate Matter (DPM) in underground metal and nonmetal mines. This most recent proposal raises many of the same issues that I discussed in those previous comments. The most important of those issues remains the generally accepted fact that the scientific database is insufficient to sustain a meaningful quantitative risks assessment (QRA) for DPM. That view, which is supported by numerous authorities, should raise important concerns within the Agency because if data insufficiencies lead to an inability to perform scientifically correct QRA, then there is no scientific basis for the specific exposure levels that lie at the heart of the current proposal.

In my prior comments, I expressed the view that the Agency's permissible exposure limits (PELs) for diesel exhaust particulate (which MSHA earlier proposed to measure as total carbon and now proposes to measure as elemental carbon) are not supported by scientific evidence. My updated review of the scientific literature confirms my prior opinion: the MSHA PELs are not scientifically supported.

As described below, the deficiencies of that database noted previously by me (and others) persist undiminished. Likewise, QRA for diesel exhaust is as scientifically unjustified and unjustifiable today as it was in1998.

My earlier submissions essentially consisted of an initial set of comments followed by two sets of updates that each extended the underlying literature review by including ever more recent publications. Despite the growth in the size and number of contributions to that literature, the conclusions of the literature review were not fundamentally altered. Similarly, my current comments update that review, but find that there is no basis to change the original conclusion.

To allow these current comments to be brief, while also not ignoring important concerns to this rulemaking, I have attached my earlier comments as appendices. Rather than reiterating the earlier arguments, I will refer to them according to appendix and page. The contents of those Appendices are as follows:

> **Appendix A**: Comments of 7/28/98 by Jonathan Borak, MD and Howard Cohen, PhD, CIH, made on behalf of the National Mining Association.

Appendix B: Comments dated 7/21/99 by Jonathan Borak, MD, prepared as an addendum to earlier comments made on behalf of National Mining Association.

Appendix C: Comments of 11/05/01 by Jonathan Borak, MD and submitted to Hon. David Lauriski on behalf of the MARG Diesel Coalition.

1. Is Quantitative Risk Assessment for DPM Possible?

In my previous comments to MSHA, I detailed deficiencies of the scientific database and expressed concerns that that database was not adequate to perform quantitative risk assessment (QRA) for diesel particulate material (DPM).

Among the issues raised were these:

a) The original proposal contained a Risk Characterization for lung cancer that misrepresented key studies and neglected others that differed with or reached alternative conclusions than MSHA (Appendix A, pages 2-6);

b) MSHA ignored the generally-accepted evidence that animal models of DPM-induced lung cancer were not applicable to humans (Appendix A, pages 6-7);

c) The MSHA risk characterization wrongly relies upon the Healthy Worker Effect to explain reduced rates or lack of increased rates of lung cancer in DPM-exposed workers, rather than addressing such reduced or non-elevated cancer rates as suggesting the absence of adverse effects (Appendix C, pages 6-10);

d) The MSHA risk assessment is qualitative, not quantitative because it is not based on quantitative exposure measurements. (Appendix A, pages 11-13).

Although my specific concerns addressed risk assessment for DPM-related cancer, they also applied to non-cancer endpoints. In support of that view, I cited the 1999 report for the Health Effects Institute (1) that found a general lack of exposure data in the relevant epidemiological studies and concluded [see Appendix B, pages 7-8].

> "Only two such studies reported any quantitative exposure data associated in some manner with the occupational epidemiologic studies."

As I pointed out then, neither of those two considered miners. Moreover, the HEI Panel further concluded that one of those two was not suitable for QRA:

> "the railroad worker cohort study has very limited utility for QRA of lifetime lung cancer risk ... the Panel recommends against using the current railroad worker data as the basis for QRA in ambient settings";

while the second had been insufficiently evaluated and was therefore of only limited value:

> "[It] may provide reasonable estimates of worker exposures to diesel exhaust, but significant further evaluation and development are needed."

Since then, there have been many debates, but essentially no new data have rectified that underlying data deficiency. For example, the just-published Proceedings of a Health Effects Institute workshop reached conclusions of even greater concern:

> "A principal limitation of epidemiologic studies of diesel exhaust exposure, whether of short-term or long-term effects, has been bias from potential exposure misclassification. Even in the occupational studies of workers exposed to diesel exhaust, exposure misclassification has been a substantial constraint in interpreting findings... Among the principal research issues are the following: - Is it possible to accurately measure diesel exposure so that quantitative estimates of the risk of lung cancer associated with diesel exposure can be made?" [(2), p. 4]

Likewise, Eric Garshick (principal author of the railroad worker study that is central to the MSHA risk assessment) presenting at that Health Effects Workshop, reiterated his public concerns that neither his own study nor any other was an adequate basis for quantifying the sort of dose-response necessary for QRA:

> "Although California has considered diesel exhaust to be a lung carcinogen with an estimable risk, this assessment is controversial. Given the lack of exposure measurements and an ill-defined linkage in the majority of these studies between job title and personal exposure ...
>
> "Although current literature identifies diesel exhaust as a health hazard, insight into a dose-response relationship is limited by factors related to both cohort selection and exposure assessment. The development of an exposure model in the existing diesel exhaust epidemiologic literature is hindered by a lack of exposure measurements upon which an exposure model can be developed, uncertainty regarding the best measurement or marker(s) indicative of exposure, and uncertainty regarding historical exposures." [(3), p.17, 21]

That deficiency has been increasingly well recognized by others outside of MSHA. Of particular note is the 2002 USEPA *Health Assessment Document for*

Diesel Engine Exhaust (4). In that document, EPA concluded that the scientific database on DPM was too uncertain to sustain QRA:

> "...the available data are considered inadequate to confidently estimate a cancer unit risk..." (p. 8-11)
>
> "Because of uncertainty in the available exposure-response data, a cancer unit risk/cancer potency for diesel exhaust has not been derived" (p. 9-24).

Accordingly, EPA published only a weight-of-evidence risk assessment, not a QRA. Likewise, EPA could make no definitive assessment of non-cancer health effects:

> "Information from the available human studies is inadequate for a definitive evaluation of possible noncancer health effects from chronic exposure to diesel exhaust" [(5), p.35]

For presumably similar reasons, ACGIH recently withdrew its proposed threshold limit value (TLV) for diesel exhaust (6). That withdrawal is striking because more than 7 years had been spent in efforts to set a diesel exhaust TLV. During that time, three different proposed TLVs (an original proposal and two subsequent revisions) were listed on its Notice of Intended Changes. In light of those 7 years of effort and deliberation, the decision to withdraw, rather than revise, reflects the fundamental weakness of the scientific data needed to set a TLV, not lack of interest in its formulation.

Thus, the past two years has seen only confirmation that the DPM database is not sufficient to allow meaningful quantitative risk assessment. No new data have been added to the database that address those deficiencies.

2. Ultimate Carcinogens and Exposure Assessment

Beyond confirming the previously noted deficiencies of the underlying database, recent studies have evidenced other important data deficiencies that previously had not been well appreciated and that now heighten awareness of the difficulties of performing DPM exposure assessments necessary for QRA. A particular concerns involves determination of the appropriate exposure metric.

If DPM is a human carcinogen, then it should be expected to contain at least one specific carcinogenic agent. For various reasons, it seems almost certain that such a carcinogen would be found in the organic carbon (OC) fraction of DPM, rather than either the elemental carbon (EC) fraction or the gaseous volatiles.

Early rodent studies found that DPM, like carbon black and titanium dioxide, caused lung cancer in rats, but not other species. Such cancers have been attributed to 'dust overload', a physical process and mechanism of disease that is

not believed to be relevant to humans (7-9). This argues that elemental carbon, essentially equivalent to carbon black, is not a potentially carcinogenic exposure in man. The Presidential Commission on Risk Assessment supports that view (10). Other studies found no evidence in rodents of lung cancer after exposure to the volatile gases in diesel exhaust (11). Thus that fraction seems also unlikely to pose cancer risks to humans. (See also Appendix A, pages 6-7).

On the other hand, the organic fraction of diesel exhaust contains specific, potentially mutagenic and carcinogenic agents, e.g., 3-nitrobenzanthrone and other nitro-PAH compounds. Recent studies have documented the presence of such agents in DPM and their activation by human enzyme systems (12,13). Likewise, DPM has been shown to upregulate cytochrome P450 1A1 (CYP1A1) leading to increased production of potentially mutagenic superoxide radicals (14). Commenting on their findings, the authors of the latter study made clear their view that PAHs, not elemental carbon were the active agents:

> "Judging from the previous reports and the present study, PAH in DPM should be responsible for the changes in these molecules and carbon nuclei of DPM are unlikely to influence the expression" (14).

Such data raise several concerns relevant to QRA.

First, if DPM exposure mediates a process leading to the formation of mutagenic oxide radicals and if that is the mechanism that leads to lung cancer, then DPM would best be described as a threshold carcinogen not amenable to linearized risk assessment models. The risk assessment models for DPM cited by MSHA rely on linearized models.

Second, and more generally, these findings suggest that if DPM exposure can cause human lung cancer, it is probably due to exposure to certain specific organic components. Most studies have not measured the organic fraction (organic carbon or OC) of DPM and none have attempted to measure the potential specific carcinogens. That failure would be of little consequence if OC exposure levels were closely related to levels of elemental carbon (EC) or total carbon (TC = EC + OC), the DPM measures that are most often reported. But, that relationship is not stable; measurements of EC and TC are now recognized as poor predictors of OC exposure. Because there are essentially no epidemiological data correlated to OC levels, and because EC and/or TC levels in such studies can not accurately predict OC, there are large and important uncertainties in the exposure assessments needed to sustain QRA. This can be restated simply: historical studies have used the wrong exposure metric for predicting lung cancer risks.

Over the past two years, an increasing number of publications have documented that EC and TC are poor estimators of OC. Much of that data has come from studies of miners. My colleagues and I published results of nearly 800 personal

and area samples from seven US mines, documenting that the EC:TC ratio varied from 0.02 to 0.73, depending on the mine, location and total DPM air level (15). Similar large variability can be inferred from studies of Australian coal mines (see Tables II and III in (16)). Data similar to those that we reported were described in an HEI study of a US gold mine (17).

But miners are not the only workers for whom EC and TC are inappropriate proxy measures of OC. A 2002 study reported comparable variability of EC, OC and TC in the diesel exhaust from railroad locomotives (18). The authors of that study concluded:

> "In this study EC constituted a range of <1-75% of the TC in the locomotive cab" (18).

In addition, researchers at the California Air Resources Board have found that the EC:OC ratio varied markedly as a given engine was subjected to different standardized dynamometer test protocols (19). The proportion of EC in DPM varied from ≈20-80%, depending on engine cycle and test protocol.

The Health Effects Institute has also recently addressed and summarized these data:

> "measurements have shown that diesel PM emissions vary greatly in composition as a result of vehicle operating conditions, engine type, fuel properties, and maintenance... Variability in PM emissions results in variations in the source profiles and, in particular, in the relative amounts of EC, OC and ultrafine PM, and possibly specific markers... Diesel emissions contain varying amounts of OC and EC. They range in composition from 90% EC data high loads (very seldom are engines run at full load) to 90% OC at idle." [(2), p. 11]

Such findings have important implications. Cancer risk assessments are extrapolations derived from estimates of relevant dose-response relationships. If exposure metrics are uncertain, then resulting calculations of individual dose (derived from those exposure measures) must be uncertain as well. And if calculated doses are uncertain, then the corresponding dose-response curves, which can not be more accurate than measured dose, will be still more uncertain. But QRA, which rely on extrapolations rather than direct measurements, cannot be more certain than the dose-response data that defines them. Thus, uncertainty in exposure assessments leads to substantially greater uncertainty in any QRA that relies upon those assessments.

The MSHA risk assessment relies on exposure measures that are not good predictors of exposure to putative carcinogens. It is derived from measurements of EC or adjusted respiratory particulate (analogous to TC) measurements that

are almost certainly not directly relevant to calculating lung cancer or other DPM health risks.

For such reasons, the MSHA risk assessment cannot be defended: it is based on the wrong exposure metric and, therefore, is not consistent with standard risk assessment practices. This conclusion, which is consistent with my earlier comments, is also consistent with the recent conclusions of the Health Effects Institute and USEPA, who argue that the current DPM database is insufficient for QRA.

MSHA should join with other responsible agencies and advisory groups by acknowledging the scientific limitations of the current DPM database for QRA, rather than forcing adoption of exposure limits that purport to be derived from a risk assessment that is scientifically indefensible.

3. Revision of the Teamsters' Exposure Assessment

In a just published report (20), Bailey et al presented a 'refinement' of the exposure assessment that was earlier utilized for QRA on lung cancer mortality in truck drivers by Steenland et al (21). This 'refinement' was a response to criticisms raised by the Health Effects Institute and others regarding the exposure assessment employed in that QRA. Although presented as an effort to address uncertainties, this effort does not clarity the issues. Among its deficiencies are the following:

a). Bailey et al accepts that there are important alternative sources of EC: "Recent studies have shown that gasoline vehicle exhaust is responsible for a substantial portion of ambient EC". In the present study, they assumed that the average proportion of EC due to diesel in the Steenland et al study was 59%. But, that study relied on a 1991 exposure survey by Zaebst et al (22), which did not provide data necessary to determine that value. Instead, Bailey et al have relied on data from other locations and times. Whether this approximation is correct (and whether it is correctly described as a beta distribution) is not directly testable or knowable.

b) A similar uncertainty involves the authors' assumption that on average, EC represents 63% of DPM by weight. That number is derived from a pooling of data from various recent studies of truck emissions. Preliminary data from California Air Resources Board indicates that the EC:TC ratio can vary widely depending on engine load, fuel type and test protocols. I also suspect that performance of older diesel engines was measurably different from that of more recent engines. Whether 63% is a correct figure for purposes of refining the Steenland et al risk assessment is not directly testable or knowable.

c). A key issue in the historical reconstruction of the Teamsters DPM exposure assessment concerns the rate of dieselization of heavy-duty trucks. Bailey et al back-extrapolated exposures to 1937 and assumed that the rate of dieselization was linear from 1937 to 1963. It is my understanding from the engine manufacturers that this is a very unrealistic assumption and not justifiable because the sharpest rate of increase was associated with creation of the national highway system in response to Eisenhower administration programs of the 1950s. From their perspective, this invalidates the study.

For several reasons, this report has no immediate impact on the risk assessment presented in the MSHA Proposed Rule.

a). The study is based on erroneous assumptions. Therefore, it is not clear that it has improved the accuracy of the prior exposure estimate.

b). Bailey et al explicitly acknowledge that 40-50% of measured EC is from other sources, mainly gasoline engines. They also acknowledge that EC is probably a marker of exposure, rather than being the "carcinogen":

> "EC is the core of diesel particulate and is the carrier of condensable organic material that is also emitted. The organic fraction of DPM includes a range of organic species ... a number of these organic species are carcinogenic... however the mechanism of injury associated with DPM is not currently known".

EC is also the marker of exposure from gasoline engines, and the exhaust from gasoline engines also contains potential carcinogens.

c). There is no *a priori* reason to assume that if lung cancers were increased among truck drivers, then that increase would be due to the non-EC fraction of DPM, rather than the non-EC fraction of gasoline engines. And, to the extent that EC exposure is a metric of miles driven or hours "on the road", it would be expected to be a covariate of any other carcinogenic exposures that were associated with miles driven or hours "on the road".

d). The study itself does not comment on exposures among miners or in underground mines. Likewise, it is not clear that these data are useful for specifically calculating lung cancer risk among miners.

Thus, it is my opinion that the recent report by Bailey et al is a flawed effort to refine the reconstruction of historical exposure among truck drivers who died in 1983. It is not directly relevant to exposures in miners or exposures in mines. It is not a risk assessment and it has no immediate impact on estimation of the carcinogenic potency of diesel particulate.

4. Human Health Data in the Final Rule

The "preamble" discussion and health effects literature cited in the proposed Final Rule present no additional or new data relevant to the human health risks of DPM. Accordingly, there is nothing in the Federal Register notice of the proposed Final Rule that alters my original opinions.

5. References

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14. Inoue K, Yoshida S, Takeda K, et al: Lung expression of cytochrome P450 1A1 as a possible biomarker of exposure to diesel exhaust particles. Arch Toxicol 76:146-151, 2002.

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16. Davies B: Diesel particulate control strategies at some Australian underground coal mines. Am Ind Hyg Assoc J 63:554-558, 2002.

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18. Liukonen LR, Grogan JL, Myers W: Diesel particulate matter exposure to railroad train crews. Am Ind Hyg Assoc J 63:610-616, 2002.

19. Ayala A: ARB's Study of Emissions from "Late-model" Diesel and CNG Heavy-duty Transit Buses. Presentation to California Natural Gas Vehicle Coalition. California: California Air Resources Board, 2002.

20. Bailey CR, Somers JH, Steenland K: Exposures to diesel exhaust in the International Brotherhood of Teamsters, 1950-1990. Am Ind Hyg Assoc J 64:472-479, 2003.

21 Steenland K, Deddens J, Stayner L: Diesel exhaust and lung cancer in the trucking industry: Exposure-response analyses and risk assessment. Am J Ind Med 34:220-228, 1998.

22. Zaebst DD, Clapp DE, Blade LM, et al: Quantitative determination of trucking industry workers' exposures to diesel exhaust particles. Am Ind Hyg Assoc J 52:529-541, 1991.

Appendix A:

Comments of 7/28/98 by Jonathan Borak, MD and Howard Cohen, PhD, CIH, made on behalf of the National Mining Association.

Comments on MSHA Proposed Rule:

Diesel Particulate Matter Exposure of Undergound Coal Miners

Fed Reg 63(68):17492-17579 (1998)

Prepared for National Mining Association

July 28, 1998

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The Mine Safety and Health Administration (MSHA) recently published its Proposed Rule for exposure to diesel particulate material (dpm) in underground coal mines (Fed Reg 63:17492-17579, 1998). We share MSHA's concerns that dpm might contribute to adverse health effects in underground miners and we believe that this possibility deserves scientific evaluation. Unfortunately, we find that the Proposed Rule inadequately addresses these concerns.

In particular, careful reading of the Proposed Rule indicates that it rests upon a series of incomplete arguments, a literature review that lacks critical rigor, and a risk assessment that is only qualitative (rather than quantitative). Accordingly, we are forced to conclude that the MSHA Proposed Rule is not based on the best available evidence and does not determine whether exposure to dpm in underground coal mines results in material impairment to health or functional capacity. Our detailed comments are presented below.

I. The section on **Risk Characterization for Lung Cancer** in the MSHA Proposed **Rule** reflects a lack of critical rigor, misrepresentation of key studies, and circular reasoning.

In its risk characterization for lung cancer, MSHA states that its conclusions are based on the results of epidemiological studies, animal studies, and genotoxicological studies. On the basis of those results, which it calls "coherent and mutually reinforcing", MSHA concludes (p.17540):

> [T]he epidemiological studies, supported by the experimental data establishing the plausibility of a causal connection, provides strong evidence that chronic occupational dpm exposure increases the risk of lung cancer in humans.

We agree that MSHA should consider such studies. But as reflected by the Proposed Rule, we find its considerations to be one-sided and lacking in critical rigor.

In particular, MSHA has: 1) selectively presented studies which support its conclusion, while ignoring others not supportive, and also failed to indicate important disagreements and disputes regarding the interpretation and meaning of studies that MSHA relies upon; 2) misrepresented the findings of a critical study; 3) used circular reasoning to support its argument that the epidemiological, animal and genotoxicological studies are "coherent and mutually reinforcing".

Our specific concerns are lustrated in the following discussion:

1. Biased Selection of **Ignoring Disagreements**

a. Among the epi l studies that MSHA identified as of particular importance to its analysis and Proposed Rule are two studies of railroad workers by Garshick et al. (1,2). MSHA describes those studies as "the two most comprehensive, complete, and well-controlled studies available" (p.17534) and "most notably ... based on far more data, contain better diesel exposure information, and are less susceptible to confounding" (p.17532).

But, MSHA failed to indicate that two reanalyses employing different analytical methods have challenged the 1988 Garshick et al. findings (2). In one, Crump et al. (3) found evidence of under ascertainment, subject selection, and inverse-dose relationships, thereby suggesting important limitations to the Garshick data. The Crump et al. study, which found no statistical association between dpm exposure and lung cancer, is not cited in the MSHA proposed rule. (By contrast, Crump et al. is discussed in detail in two studies that MSHA indicates it relied upon, Stayner et al. (4) and the California EPA risk assessment (5)).

In the second reanalysis, Cox (6) employed analytical methods developed in the AI-and-statistics ("artificial-intelligence-and-statistics") literature and concluded that the Garshick et al. data did not support a causal association between dpm concentration and occupational lung cancer. MSHA cites the Cox study without detail, merely listing it as one of several that raised questions "as to whether the evidence linking dpm exposure with an excess risk of lung cancer demonstrates a causal connection" (p.17539).

Considering MSHA's statement that the 1988 Garshick et al. study was of particular importance for justifying its Proposed Rule, failure to discuss two detailed reanalyses that disagreed with that study's conclusions and MSHA's interpretation is an important omission.

MSHA details the content of a "comprehensive statistical meta-analyses of the epidemiological literature" performed by Bhatia et al. (7) and then concludes the discussion with a quote from the l a et al. (p.17540):

> "[T]his meta-analysis supports a causal association between increased risks for lung cancer and exposure to diesel exhaust."

MSHA neglects to mention the differing opinion expressed in an accompanying editorial by DT Silverman, Principal Investigator of the on-going NCI-NIOSH study of dpm in non-metal mines. In that editorial, Silverman states (8):

> "Bhatia et al. conclude that the data support a causal association between diesel exhaust and lung cancer in humans. Has science proven causality beyond any reasonable doubt? Probably not. The repeated finding of small effects, coupled with the absence of quantitative data on historical exposure, precludes a causal interpretation".

MSHA cites the Silverman editorial without detail, listing it as one of several that raised questions "as to whether the evidence linking dpm exposure with an excess risk of lung cancer demonstrates a causal connection" (p.17539).

In light of the importance that MSHA gives to Bhatia et al its failure to discuss the Silverman editorial which specifically disagrees with MSHA's view is a significant omission which again reflects MSHA's underlying bias.

2. Misrepresentation of Research Findings

MSHA discusses a yet unpublished report by Stayner et al. (4) which summarized a number of previous quantitative risk assessments on dpm and lung cancer. With respect to that report, MSHA presents the following summary and interpretation (p.17541):

> [E]stimates of the exact degree of risk vary widely even within each broad category ... However, <u>all</u> of the very different approaches and methods published so far, as described in Stayner et al., have produced results indicating that levels of dpm exposure measured at some underground mines present an unacceptably high risk of lung cancer" [emphasis added by MSHA].

But the MSHA statement is wrong. Stayner actually describes a complex risk assessment by Crump et al. (3) that reached an opposite conclusion. That risk assessment was published as an appendix to the EPA risk assessment (9). Following is Stayner's statement describing the Crump et al. study:

> "More than 50 analyses of the relationship between exposure to dpm and lung cancer mortality were conducted using 5 different markers of exposure, 5 ways of accumulating past exposures, several subgroups of the cohort based on job in 1959, and both relative and absolute risk models. None of the analyses revealed a significant positive relationship between dpm exposure and lung cancer, and some of the analyses produced negative exposure-response relationships" [emphasis added].

Stayner further states that after errors were found in Crump's methodology, Crump "acknowledged the errors and repeated the analysis", but again no significant exposure-response relationships were found in most of the models. (This is corroborated by California EPA: "the investigation determined in parallel calculations with Dr. Crump, that the particular approach of the report still did not lead to a significant positive relationship" (5)

In light of the importance that MSHA gives to the Stayner et al. study, misrepresentation of its contents seems a significant error. It is even more striking that MSHA wrongly emphasized that "all ... approaches and methods" had yielded results indicating that dpm exposure at some underground mines posed unacceptably high risks.

3. Reliance on Circular Reasoning

In its **Characterization of Risk for Lung Cancer**, MSHA relies heavily upon its determination that the results of epidemiological, animal and genotoxicological studies are "coherent and mutually reinforcing" (p.17540):

> Results from the epidemiological studies, the animal studies, and the genotoxicological studies are coherent and mutually reinforcing. After considering all these results, MSHA has concluded that the epidemiological studies, supported by the experimental data establishing the plausibility of a causal connection, provide strong evidence that chronic occupational dpm exposure increases the risk of lung cancer in humans

But it is not obvious that the scientific literature actually contains such "coherent and mutually reinforcing" results. To the contrary, it seems that such coherency and reinforcement is actually a product of circular reasoning practiced by MSHA. This may be best seen by restating the arguments made by MSHA in the

proposed rule.

3a. Epidemiological data

MSHA indicates that there much epidemiological data, but that most of the individual studies are not very good. For example

> Since none of the existing human studies is perfect and many contain major deficiencies, it is not surprising that reported results differ in magnitude and statistical significance. Shortcomings identified in both positive and negative studies include: possible misclassification with respect to exposure; incomplete or questionable characterization of the exposed population; unknown or uncertain quantification of diesel exhaust exposure; incomplete, uncertain, or unavailable history of exposure to tobacco smoke and other carcinogens; and insufficient sample size, dpm exposure, or latency period. (p.17532)

> ... that 38 of 43 studies showed any excess risk of lung cancer associated with dpm exposure may itself be a significant result, even if the evidence in most of those 38 studies is relatively weak. (p.17533) [emphasis added]

Moreover, MSHA notes that none of the individual epidemiological studies provides sufficient evidence that dpm causes human lung cancer:

> MSHA recognizes that no single one of the existing epidemiological studies, viewed in isolation, provides conclusive evidence of a causal connection between dpm exposure and an elevated risk of lung cancer in humans. (p.17539)

MSHA ultimately describes the epidemiological results as suggesting the "plausibility of a causal interpretation for relationships" between dpm and human lung cancer. Such "plausibility", MSHA argues, is supported by the results of animal studies:

> The fact that dpm has been proven to cause lung cancer in laboratory rats is of interest primarily in supporting the plausibility of a causal interpretation for relationships observed in the human studies. (p.17540)

Thus, MSHA concludes that the epidemiological studies suggest an association between dpm and lung cancer, but that suggestion is made credible in light of the animal data.

3b. Animal data

Chronic exposure to dpm causes lung cancer in rats, a finding "confirmed in two strains of rats and in at least five laboratories", but such effects have not been demonstrated in other species. Moreover, pulmonary response to dpm in primates differs from that of rats. Therefore, MSHA concludes that extrapolation of risk from rats to humans is problematic:

> The conflicting results for rats and hamsters indicate that the carcinogenic effect of dpm exposure may be species dependent. Indeed, monkey lungs have been reported to respond quite differently than rat lungs to both diesel exhaust and coal dust. Therefore, the results from rat experiments do not, by themselves, infer any excess risk due to dpm exposure for humans. (p.17536)

Accumulated evidence also indicates that strains of rats which develop lung cancer following chronic dpm exposure also develop identical cancers following exposure to non-genotoxic sub-micron particulates of carbon black and titanium dioxide. MSHA agrees that this suggests that dpm-induced lung cancer in rats is not due to the genotoxicity of diesel exhaust:

> Therefore, it appears that the toxicity of dpm, at least in some species, may result largely from a biochemical response to the particle itself rather than from specific effects of the adsorbed organic compounds. (p.17537)

MSHA also discusses evidence that dust overload is the causal mechanism for rat lung cancers after exposure to dpm, carbon black and titanium dioxide. Data suggesting that dust overload does not occur in humans is also discussed. These data have led others, such as the Presidential/Congressional Commission on Risk Assessment and Risk Management ("Commission"), to conclude that the rat lung cancer model may not be relevant to human cancer risk assessment. For example, the Commission cautions that "Regulatory agencies should distinguish between tumor responses that are predictive and those that are not" and specifically refers to rat lung tumors after the overwhelming of clearance mechanisms as an example of "rodent tumor mechanisms that may not be relevant to human cancer risk if they are the only responses observed" (10).

MSHA, however, offers no evidence to support its view that the rat model is relevant, concluding simply that:

> MSHA is not aware of any evidence that a mechanism of carcinogenesis due to fine particle overload is inapplicable to humans. Studies carried out on rodents certainly do not provide such evidence. (p.17537)

We are concerned that MSHA maintains this view precisely because there is no evidence. Ultimately, MSHA argues that the rat lung cancer model is relevant to humans because of the epidemiological studies:

> The human epidemiological data, however, indicate that humans comprise a species that, like rats and unlike hamsters, suffer a carcinogenic response to dpm exposure. Therefore, MSHA considers the rat studies at least relevant to an evaluation of the risk for humans. (p.17536)

Thus, despite lack of a direct connection and accumulated animal evidence to the contrary, MSHA argues that epidemiological data justify its view that the rat lung tumor studies are relevant mechanistically to humans.

3c. Genotoxicity data

MSHA indicates that diesel soot is genotoxic in a variety of test systems, but also allows that there are other data suggesting that lung cancer risks of diesel exhaust in animals is unrelated to genotoxic mechanisms. The MSHA discussion of this negative data neglects a number of important studies (11-13). Those negative studies has led others, such as California EPA, to conclude that "the role of the genotoxic constituents of diesel exhaust in the development of rat lung tumors is as yet undefined" (5).

Nevertheless, MSHA speculates that the genotoxic effects of dpm are "masked" by dust overload:

> Due to the relatively high doses administered in the rat studies, it is conceivable that an overload phenomenon masks or parallels other potential routes of cancer. It may be that effects of the genotoxic organic compounds are merely masked or displaced by overloading in the rat studies ... Particle overload may provide the dominant route to lung cancer at very high concentrations of fine particulate, while genotoxic mechanisms may provide the primary route under lower-level exposure conditions. (p.17537)

MSHA continues to speculate about possible genotoxic mechanisms:

> Even if the genotoxic organic compounds in dpm were biologically unavailable and played no role in human carcinogenesis, this would not rule of the possibility of a genotoxic route to lung cancer (even in rats) due to the presence of dpm particles themselves... Therefore, the carbon black and titanium dioxide studies cited above do not prove that dpm exposure has no incremental, genotoxic effects ... (p.17537)

Thus, the MSHA genotoxicity argument consists largely of speculation that dpm might cause cancer via a genotoxic mechanisms because existing evidence cannot disprove the theory MSHA seemingly ignores the lack of direct evidence and the consistency of contrary evidence.

3d. Summary

MSHA argues that the research findings of epidemiological, animal, and genotoxicological studies on dpm and lung cancer are "coherent and mutually reinforcing". This is not so. But to the contrary, this is not so.

> The "relatively weak" epidemiological studies suggest only "the plausibility of a causal interpretation". To MSHA, that possibility is made credible because "dpm has been proven to cause lung cancer in laboratory rats".
>
> But, the rat experiments "do not, by themselves, infer any excess risk due to dpm exposure for humans". To MSHA, that possibility is made credible in light of the epidemiological studies.
>
> The genotoxicological studies lead only to speculation of possible mechanisms.

Whether MSHA's concerns and speculations are correct, it seems clear that the Agency has built its logical argument without an anchor point. The cited data and their inter-connections are interesting and provocative, but they are clearly not ""coherent and mutually reinforcing". **The section on Risk Characterization for Lung Cancer in the MSHA Proposed Rule reflects a lack of critical rigor,** misrepresentation of key studies, and circular reasoning.

II. There is little evidence to support MSHA's view that health effects associated with ambient exposure to $PM_{2.5}$ are relevant to risk assessment for and regulation of diesel

exhaust.

A substantial part of the MSHA Risk Assessment considers "Health Effects Associated with Fine Particulate Matter in Ambient Air". For example, MSHA states in III.2.a.iii:

> Since dpm is a type of respirable particle, information about health effects associated with exposure to respirable particles in general, and especially to fine particulate matter, is certainly relevant, even if difficult to apply directly to dpm exposures. (p.17528)

MSHA recognizes two difficulties in utilizing such information for risk assessments of miners with occupational dpm exposure: 1 exposures to fine particulates in air pollution studies are not specific to dpm (or any other single kind of particulate); and, 2) observations of effects in the general population do not necessarily apply to the population of miners. Despite those difficulties, however, the Agency concludes that "there are compelling reasons to consider this body of evidence".

We do not dispute that it is appropriate for MSHA to consider such data, but we disagree with MSHA's discussion and conclusion in several ways. First, as discussed below, we believe that MSHA has failed to note a variety of technical difficulties that make the utilization of such information problematic. Secondly, and more importantly, we disagree with MSHA's conclusion that:

> [T]he excess risk of death that has been linked to pollution of the air with fine particles like dpm is clearly a "material impairment" of health or functional capacity within the meaning of the act. (p.17539)

In particular, we do not agree that the ambient air pollution studies referenced by MSHA have linked "pollution of the air with fine particles like dpm" [emphasis added] to excess risks of death or chronic lung disease. The basis for our disagreement can be summarized as follows:

MSHA argues that the ambient pollution literature for $PM_{2.5}$ is relevant to dpm because dpm is mostly less than 1.0 micron in size:

> A new NAAQS has now been established for "fine particulate matter" that is less than 2.5 microns in size ... dpm is mostly less than 1.0 micron in size. It is, therefore, a fine particulate. (p.17510)

MSHA appears to regard all particulates smaller than 2.5 um as equivalent. We believe that this approach is not appropriate.

There are well recognized differences in size and distribution between dpm and $PM_{2.5}$. As illustrated in Figure II-1 of the proposed rule (p.17504), the mass median aerodynamic diameter of dpm is between 0.1-0.3 um (e.g., 14-17). By contrast, ambient particulate matter is much more heterogeneous with regard to size. The cut-off diameter of size selective samplers is not sharp and samples collected with $PM_{2.5}$ samplers actually contain a significant proportion of particles greater than 2.5 um (18,19). DPM and other ultra-fine particulates represent only a small proportion of ambient particulate samples: it is estimated that dpm represents less than 4 percent of total suspended particulate emissions (20).

Such size and distribution differences have important implications for the anticipated health effects of particulate exposure. For example, MSHA's concern that dpm exposure leads to chronic cough, chronic phlegm, and wheezing reflects mainly tracheobronchial effects. But there are extensive research studies documenting that regional deposition, retention and biopersistence of inhaled particles differ significantly according to particle size, especially very large and very small (i.e., less than 0.5 um) particles (e.g., 18,21-24). Of particular relevance, studies in humans and other species have found that tracheobronchial deposition increased by 2-10 fold as particle size increased from 0.8 to 6.0 um (25). Thus, air pollution studies, even those that considered "fine" particulate matter less than 2.5 um, are neither quantitatively predictive of nor inherently relevant to the physiological effects of sub-micron particulates. such as dpm, on the tracheobronchial tree.

MSHA has essentially ignored the differences between sub-micron dpm and air pollution-related $PM_{2.5}$ particulates which are the focus of EPA's NAAQS. Likewise, MSHA has failed to establish a credible basis for linking the $PM_{2.5}$ literature to quantitative risk assessments of exposure to dpm.

In addition, MSHA has failed to acknowledge the various concerns expressed by EPA regarding the data underlying the new NAAQS and their ability to predict and explain the biological effects of particulate exposures:

> [T]here remains uncertainty regarding the shapes of PM exposure-response relationships; the magnitude and variability of risk estimates for PM; the ability to attribute observed health effects to specific PM

> constituents; the time intervals over which PM health effects (e.g., shortening of life) are manifested; the extent to which findings in one location can be generalized to other locations; and the nature and magnitude of the overall public health risk imposed by ambient PM exposure. While the epidemiology data provide support for the associations mentioned above, understanding of underlying biologic mechanisms has not yet emerged.

In summary, MSHA has failed to address important physiological implications of size differences between dpm and $PM_{2.5}$, the limited evidence linking $PM_{2.5}$ specifically to adverse health effects, and persistent uncertainties regarding quantitative relationships between exposure to particulate matter and health effects. **There is little evidence to support MSHA's view that health effects associated with ambient exposure to $PM_{2.5}$** are relevant to risk assessment for and regulation of diesel exhaust.

III. MSHA's determination that methods do not exist to accurately measure dpm is incorrect and results in a Risk Assessment which cannot achieve quantitative conclusions.

Critical to the MSHA Risk Assessment and Proposed Rule is the Agency's determination that it is not possible to accurately measure dpm exposure:

> The Agency is not confident that there is a measurement method for dpm that will provide accurate, consistent and verifiable results at lower concentration levels in underground coal mines. (p.17498)

That determination leads to two far reaching implications: first, that the MSHA Risk Assessment cannot achieve quantitative conclusions; secondly, that MSHA cannot establish exposure limits or provide quantitative exposure guidelines for dpm. These two implications are discussed below.

1. **MSHA Risk Assessment is Qualitative, not Quantitative**

MSHA's Risk Assessment does not reach quantitative conclusions because it is not based on measured levels of exposure. Instead of using accepted risk assessment methods (e.g., 10,26-28) to generate quantitative risk characterizations and thereby estimate risk to miners exposed at various dpm levels, MSHA has simply concluded that:

> [M]iners subjected to a lifetime of dpm exposure at concentrations we presently find in underground mines face a

> significant risk of material impairment to their health (p.17494)

Because the MSHA Risk Assessment is not based on exposure measurements, its conclusions are only qualitative. For the same reasons, MSHA's use of the term "significant" in the above quoted sentence has no statistical meaning.

As discussed below, we do not agree that dpm measurements cannot be made accurately and consistently. More importantly, we find that MSHA has failed to adequately justify its own negative conclusions regarding use of dpm exposure measurements. This is particularly striking in light of MSHA's acknowledgment that various international regulatory and advisory agencies have already or are preparing to adopt explicit dpm exposure limits.

Moreover, the Proposed Rule is internally inconsistent on this issue. On the one hand, MSHA states that it is not confident in the ability to measure dpm in underground coal mines, while on the other hand it argues that currently measured levels are too high:

> At exposure levels currently observed in underground mines, many miners are presently at significant risk of incurring these material impairments over a working lifetime. (p.17495)

In short, we find that MSHA has failed to adequately justify its opinion that quantitative dpm measurements are not possible, has failed to reconcile that view with the opinions and actions of other international agencies, and has failed to recognize the self-contradictions of its own arguments. We do not agree with MSHA that a quantitative risk assessment for dpm cannot and should not be performed. We are surprised by the Agency's failure to calculate a range of risk estimates thereby allowing its assessment to be evaluated and critiqued in light of possible measurement uncertainties. We believe that the Agency should at least use sensitivity analysis to estimate the impact of such uncertainty on a quantitative risk assessment.

As published in the Proposed Rule, **the MSHA Risk Assessment is inappropriately and unnecessarily qualitative** and deviates below standards and guidelines published by the National Research Council, Presidential/Congressional Commission on Risk Assessment and Risk Management, EPA, and others.

2. Adverse Effects of MSHA's Failure to Establish Exposure Guidelines

Because MSHA "is not confident" that dpm can be accurately measured, the Proposed Rule relies on the use of best-available technology (BAT) to control particulate emissions originating from diesel-powered equipment used in underground coal mines. MSHA explicitly rejects the alternative approach of establishing exposure limits or guidelines:

> The agency also spent a considerable amount of time studying whether it could simply propose a concentration limit for dpm in underground coal mines ... However ... the Agency believes that the best approach for the underground coal sector would be one which does not require measurement of ambient dpm levels to ascertain compliance or noncompliance. (p.17498)

The decision by the Agency to not establish dpm exposure limits or exposure guidelines will lead to important negative outcomes: 1) mine operators will be forced to use only one control technology to reduce dpm emissions, rather than utilizing those methods that are the most cost-effective and best reduce employee exposures; 2) mine operators and their employees will have no way to judge the effectiveness of engineering controls in reducing exposures to dpm; 3) there will be little or no incentive for mine operators to collect exposure data that would sustain long-term epidemiologic studies of possible dpm-induced adverse effects to employees.

Moreover, this approach is inconsistent with the recommendations found in the MSHA "Toolbox" which outlines ways to reduce dpm exposure by means of ventilation and engineering controls. We agree with MSHA that the recommended "Toolbox" strategies would provide potential benefits to workers in mines where dpm exposure levels are excessive. Adoption of the Proposed Rule will decrease incentives to utilize such "Toolbox" strategies.

Considering the negative impact of MSHA's determination that dpm exposure measurements cannot provide "accurate, consistent and verifiable results", we urge the Agency to re-evaluate the basis for its conclusion. We particularly note that other respected agencies, including the ACGIH TLV Committee (29), the Canadian Centre for Mineral and Energy Technology, and the German government (p.17518) have either adopted explicit exposure limits supported by quantitative exposure measurements or are moving forward to establish such limits.

Unlike MSHA, we believe that appropriate sampling and analytical methodology do currently exist to permit accurate, consistent and

verifiable measurements of dpm. In fact, we are currently using several such methods in a study of diesel exhaust exposure in non-metal mines. Likewise those methods are in use as part of the NIOSH-NCI study described in the Proposed Rule. Our disagreement with the MSHA determination about dpm measurement is discussed below.

Exhaust emissions from diesel engines consist of a mixture of gases and complex particulates. The major gas emissions include nitrogen monoxide, nitrogen dioxide, sulfur dioxide, formaldehyde and carbon monoxide. Each of those gases has established methods for exposure monitoring and each has accepted exposure limits (such as OSHA and MSHA PELs) that address occupational exposures. Particulate emissions consist of an elemental carbon core surrounded by organic molecules including polycyclic aromatic hydrocarbons. Cantrell and Rubow (14,15,30) and others (31) have shown that the vast majority of diesel exhaust emissions exist as a submicron aerosol, even after agglomeration has occurred.

The concerns raised by MSHA in the Proposed Rule concerning the accurate measurement of diesel exhaust fall into three general areas: 1) will elemental carbon from coal dust interfere with the collection of dpm?; 2) will current sampling techniques collect all of the dpm present?; 3) will environmental tobacco smoke or other substances (e.g. oil mist) interfere with the analysis of dpm? As discussed below, each of these concerns should not inhibit the collection of exposure data. Other potential concerns, such as whether the NIOSH analytical method #5040 for dpm is adequately sensitive and whether analyses are sufficiently simple and available at a reasonable cost have been answered by MSHA in the Proposed Rule: the NIOSH method can detect as little as 1 $\mu g/m^3$ for a full shift air sample and the analysis is relatively simple and available at a price of $30-50 per sample (p.17507).

1. **Will elemental carbon from coal dust interfere with the collection of dpm?**

Testing of aerosol sampling of dpm, coal dust, and combinations of the two have been conducted in laboratory and field settings (14). Laboratory testing demonstrated that nearly all dpm was below 1 µm with a mass median diameter (MMD) of 0.15 µm. By contrast, coal dust was nearly all supermicrometer in size with a MMD of 3-10 µm. These findings were verified in field studies of coal mines using both electric and diesel equipment. Electric mines (which, therefore, had no dpm) demonstrated a single aerosol

distribution with a MMD of about 7 µm, while diesel mines had a bimodal aerosol distribution with dpm having a MMD of approximately 0.15 µm.

MSHA indicates concern that if 10% of coal dust were submicron in size it might interfere with the analysis of dpm (p.17506). Our first response, in light of the findings of Cantrell and Rubow, is that MSHA's estimate of 10% submicron coal dust is too high. But even if MSHA were correct, that would lead to a positive interference that might overstate the true value of dpm. Such an error would lead to overprotection, not underprotection of workers.

Ultimately, if the collection of submicron coal dust proved problematic to some mines, it could be addressed by means of a correction factor reflecting the ratio of total submicron carbon to elemental submicron carbon aerosols: the presence of coal dust would lead to higher than expected elemental carbon levels.

2. Will current sampling techniques collect all of the dpm **present?**

MSHA expresses concern that, because up to 20% of dpm might be larger than 1 µm, use of NIOSH Method #7040 for the collection of dpm might underestimate exposure. The agency cites the work of Vuk et al. (32) in support of its concerns. The Vuk et al. report describes a laboratory study which evaluated dpm from equipment operating in 13 different modes. In 11 of those 13 modes, more than 90% of the particles were less than 1 µm. Only two of 13 operating modes yielded more than 10% of dpm larger than 1 µm: in both cases, the exhaust temperature was very low (<200° C) and particle concentrations were the lowest of all in the 13 studied operating modes. Thus, we find that the results of Vuk et al. do not support MSHA's concerns.

In addition, laboratory and field studies by Cantrell and Rubow in both coal and metal/non-metal mines (14,15) have clearly shown that there are not significant amounts of dpm greater than 1 µm that would fail to be collected using NIOSH Method #7400. The agency itself has previously stated: "...that over 90 percent of diesel particulate is less than 0.8 micrometers in aerodynamic diameter ..." (33)

Accordingly, we believe that the most likely bias resulting from use of NIOSH Method #7040 would be overestimation of

the true concentration of dpm, due to the presence of submicrometer-size coal dust as discussed above. Any underestimation of dpm due to supermicrometer-sized aerosols can be expected to be insignificant (<10%). On balance, we believe that if any collection errors occurred, they would lead to overprotection, not underprotection of workers.

3 Will cigarette smoking or other substances (e oil mist) interfere with the analysis of dpm?

Under some collection scenarios, environmental tobacco smoke (ETS) might cause positive interference with the analysis of dpm. Some portion of ETS may be less than 1 μm and can be analyzed as organic carbon using NIOSH Method #7040. Woskie et al. (34) reported that for dpm-exposed workers, measured exposure to respirable particulate matter differed depending on their smoking habits. However, these investigators did not use an impactor to eliminate supermicrometer aerosols, and they used only a gravimetric analysis to measure dpm.

By contrast, Zaebst et al. (35) performed similar studies, but used an impactor to separate submicrometer aerosols and a thermal-optical analysis method to separate elemental carbon from organic carbon exposures. That study found no significant increase in worker exposures to dpm based on smoking habits. Zaebst et al. estimated that ETS would contribute no more than 10 $\mu m/m^3$ to total dpm exposure.

It is unclear whether there are other substances that could positively interfere with the collection and analysis of dpm. However, the methods used by Zaebst et al. to compare ratios of total and elemental carbon should differentiate dpm from other exposures in mines with unique confounders.

3. Summary

In summary, MSHA's determination that there are no accurate, consistent and verifiable methods to measure dpm is not adequately justified in the Proposed Rule. Moreover, there is evidence the MSHA determination is not correct. Because of that determination, the MSHA Risk Assessment is not quantitative and fails to meet generally accepted risk assessment standards. MSHA is also thereby unable to propose exposure limits or exposure guidelines so that mine operators would be able to assess the effectiveness of various dpm control strategies.

Accordingly, we believe that there is little evidence to support

MSHA's determination that dpm measurements are not feasible, that the determination renders the MSHA risk assessment deficient, and that it also prevents mine operators from evaluating the adequacy of dpm control strategies including those proposed in the MSHA "Toolbox".

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Appendix B:

Comments dated 7/21/99 by Jonathan Borak, MD, prepared as an addendum to earlier comments made on behalf of National Mining Association.

The following comments are an addendum to my earlier comments on the risk assessment contained in MSHA's Proposed Rules on exposure to diesel particulate matter (dpm). The primary purpose of this addendum is to address questions about the adequacy of epidemiological studies linking dpm and lung cancer in miners, particularly in light of comments made by MSHA's Jon Kogut during hearings held May 13 in Albuquerque. A second objective is to reconsider Mr. Kogut's comments and the MSHA Proposed Rules in light of the very recent Health Effects Institute report on Diesel Emissions and Lung Cancer.

Epidemiological Studies cited by Kogut

In his May 13 comments (see Transcript of Proceedings, 5/13/99, p.59-63), Jon Kogut stated that MSHA had identified six studies

> "that look for an association between miners' exposure to diesel particulate or miners and an increased risk of lung cancer"

which he then briefly discussed Those studies were cited:

> "to clear up the impression ... that we were not ... taking into account any studies having to do with mining and that we were relying entirely on ... rat studies ... whose applicability to humans might be questioned" (Transcript, p.63).

The studies can be found summarized in Tables III-4 and III-5 of the proposed rules for Underground Coal Miners [Fed Reg 63:17545-17554, 1998] and Underground Metal and Nonmetal Miners [Fed Reg 63:5812-58180, 1998].

In other words, the studies cited by Kogut were included by MSHA in the Proposed Rules because they apparently support the contention that dpm causes lung cancer in miners. However, a closer examination of those studies indicates that they do not provide such support:

- None of the six studies contains exposure assessment data;
- None distinguished exposed vs. non-exposed miners;
- Where data are provided, diesel-exposed miners represented only a minority of the total mining personnel included in each study.

In addition, other important limitations to the various studies include (but are not limited to) generally imprecise job categorizations, failure to consider types of mining performed, failure to consider important confounding exposures, and neglect of secondary work exposures. The following discussion is provided to clarify those limitations and deficiencies.

Boffetta et al. (1)

Background: This study was conducted by American Cancer Society (ACS) volunteers using self-administered questionnaires. There were 476,648 men 40-79 years of age enrolled in the study. Every two years, follow-up by the ACS volunteers determined whether subjects were alive or dead. Death certificates were obtained to document causes of deaths.

Occupational assessment: Three questions identified: 1) current occupation; 2) last occupation, if retired; 3) job held for longest period of time. Occupations were then coded according an "ad hoc two-digit classification ... a more specific classification ... was impractical for the large number of ambiguous responses derived from a self-administered questionnaire".

DPM Exposure assessment: Exposure at work or daily life to diesel engine exhaust and eleven other groups of substances were "investigated" by questionnaire only. The authors stress that "quality of information on exposure is a major problem in self-administered questionnaires". Efforts were not taken to determine the accuracy of self-reported exposures.

Results for dpm exposure based on self-reports were:

DPM Exposure in	All Subjects
Exposed to dpm	**62,800**
Not exposed to dpm	**307,143**
Question not answered	**92,038**

Description of miners: A total of 1233 subjects were identified as miners. No information was provided regarding the types of mining performed (e.g., underground) or the ores mined (e.g., uranium, copper), although the analysis included adjustment for self-reported exposure to "coal and stone dusts" and asbestos.

Only a small proportion of the miners reported exposure to dpm:

DPM Exposure in Miners	
Exposed to dpm	**14.4 %**
Not exposed to dpm	**41.4 %**
Question not answered	**44.2 %**

Lung Cancer Analyses: Analysis of the association between lung cancer and mining was performed on the total group of miners. Analysis did not compare risk of lung cancer in dpm exposed vs. not exposed miners because "too few exposed cases were observed". However, when such an exposed-vs-not-exposed analysis was performed on truck drivers, there was "no overall association" with dpm.

Other points of interest: The association between dpm and lung cancer was confounded by age, smoking, and other occupational exposures (e.g., asbestos), although only a limited number of such exposures were determined. No association was found between dpm exposure and mortality for non-neoplastic pulmonary diseases.

Waxweiler et al (2)

Background: This study was conducted by NIOSH to evaluate the risks of lung cancer in a cohort of potash miners "exposed during their underground employment to no known carcinogens in the ore". Death certificates were obtained for 98.9% of the cohort who died between 1940 and 1967.

Occupational assessment: Study included miners and millers who had worked at least one year at any of eight potash mining companies. Employment records were reviewed.

DPM Exposure assessment: One of the potash mines had used diesel engines as the "major energy source" since 1949 and another since 1957. Apparently the other six mines did not use diesel engines. There were no specific measures of diesel exposure.

Description of miners: Subjects were divided on the basis of employment records into two groups. One group comprised 2743 men who had at least one year of underground potash work and less than one year of surface potash work. The second group comprised 1143 men who had at least one year of surface potash work and less than one year of underground work. The underground cohort was also "subdivided on the basis of which men had worked (and when)" in the two mines with diesel engines.

Lung Cancer Analyses: No statistically significant excess of lung cancer was demonstrated among the groups of potash workers, even when duration of employment was considered. The dpm-exposed miners contributed 19.1% of the total person years of the study. "No cause of deaths were significantly different between miners who worked in dieselized mines and those who worked in other mines".

Other points of interest: Mortality rates from non-neoplastic pulmonary diseases did not differ between dpm-exposed and not exposed miners.

Benhamou (3)

Background: This case-control study of male lung cancer patients was conducted in France with funding from US NCI. There were 1260 cases of proven lung cancer and 2084 controls with diseases not related to tobacco. The study was

performed "principally to study the effect of exposure to tobacco on the occurrence of lung cancer."

Occupational assessment: A "complete occupational history was recorded ... respondents were asked to give their occupations, from the most recent to the first, with the corresponding duration (at least one year)."

DPM Exposure assessment: Exposure to dpm was not considered in this study.

Description of miners: A total of 22 cases and 20 controls were identified as "miners, quarrymen" but the mining conditions (e.g., underground) and ore mined (e.g., uranium, coal) were not recorded in this study.

Lung Cancer Analyses: There was a statistically significant association between lung cancer and work as "miners, quarrymen", but there was "no evidence of an increase in risk with duration of exposure". Specific associations between lung cancer and dpm exposure were not evaluated.

Lerchen et al. (4)

Background: This case-control study was conducted to study the incidence of lung cancer among several ethnic groups in New Mexico. A total of 771 controls were identified by screening randomly selected telephone numbers and from the HCFA roster of Medicare participants. Information was provided by next of kin in about 50% of cases, whereas 83% of controls provided their own information.

Occupational assessment: Study questionnaire "obtained a lifelong occupational history". For the analyses, "the measure of employment experience was whether an individual was 'ever employed' for at least 1 year in an industry or occupation."

DPM Exposure assessment: There was no specific measure of diesel exposure. The authors state that "in the context of this population-based, case-control study, use of job title was the only feasible approach for classifying exposure status ... grouping by exposure was thus generally not possible. "

Description of miners: A total of 31 miners were identified who specifically had "underground experience". Of those, 7 were uranium miners. The other 24 mined copper, lead, zinc, gold and silver, molybdenum, coal, clay or potash. Further details were not provided.

Lung Cancer Analyses: An association was found between mining and lung cancer. Odds-ratios were the same for those with and without uranium mining experience. Specific associations between lung cancer and dpm exposure were not evaluated.

Other points of interest: No increased risk of lung cancer was found for jobs that involved asbestos exposure.

Siemiatycki et al. (5)

Background: This case-control study was conducted to study the association between 20 sites of cancer and occupational exposure to ten types of exhaust and combustion products. There were 3726 hospitalized male cancer patients. Patients with each type of cancer defined a "case series" which was compared to patients with other cancers, the "controls".

Occupational assessment: An "in-depth interview elicited a detailed job history."

DPM Exposure assessment: There was no specific measure of diesel exposure. The authors state that "a team of chemists and hygienists examined each completed questionnaire and translated each job into a list of potential exposures ... for each subject, the data set comprised semi-quantitative information on the degree of exposure." Moreover, "relatively high exposures to diesel exhaust were attributed" to persons who worked as miners (emphasis added).

Description of miners: The miners were not described. Based on data contained in Table 3 of the study report, 36 "mining and quarrying" workers were regarded as diesel-exposed. The total number of miners and the types of mining performed were not reported.

Lung Cancer Analyses: An association was found between mining and lung cancer. With respect to presumed dpm exposure, the analysis found that there were "higher risks among those with short exposure than among those with long exposure", thus suggesting an inverse or negative dose-relatedness.

Other points of interest: The authors concluded that there was "no compelling evidence that diesel particle extracts are more potent than gasoline exhaust extracts."

Swanson et al (6,7)

Background: This population-based case-control study was conducted in Detroit to evaluate occupational risk factors for cancer. The study included men 40-84 years of age. There were approximately 3900 lung cancer patients and 1950 patients with colon or rectal cancer, who served as controls. (The numbers of subjects differed between the two reports). Information was obtained by telephone interview.

Occupational assessment: A "lifetime work history" was obtained including "occupational and industry titles of all jobs ever held, a complete description of the duties performed, the dates each job began and ended, and whether the job

was-full or part-time." Usual occupation and industry were defined by "summing the total number of months a person was employed in a specific industry or occupation over the entire work history and then selecting the occupation and industry for which the person had accumulated the largest number of months of exposure".

DPM Exposure assessment: The authors state "no direct information has been obtained regarding specific exposures ... in order to reduce interview time for the large number of interviews conducted, exposure data were not obtained" (8). They also admit that, "many of the epidemiological studies [of dpm exposure] suffer from lack of exposure data, as does this study". Instead of exposure data, the authors grouped occupations and industries according to "probable similarities in work exposures ... based on review of the literature and consultations with an industrial hygienist and an occupational physician" (emphasis added).

Description of miners: The miners were not described. The first report (6) included 19 cases and 6 controls who were "excavating and mining workers", 23 cases and 7 controls from the "mining industry group", and 16 cases and 5 controls who were "mining machine operators". The "mining machines" were not described. The extent of overlap among those categories was not indicated. The second report (7) included 156 cases and 99 controls who were "coal miners". No other miners were included in that study.

Lung Cancer Analyses: An increased risk was found between lung cancer and mining, coal mining, and operating mining machines. There was no analysis of the association of lung cancer and exposure to dpm.

Other points of interest: The authors describe the association found between concluded that "there is no compelling evidence that diesel particle extracts are more potent than gasoline exhaust extracts."

Summary

As detailed above, the six studies cited by Mr. Kogut and included in the MSHA Proposed Rules do not directly address concerns regarding associations between dpm and lung cancer in miners. By contrast, the only one of the studies that specifically compared dpm-exposed and not exposed miners, Waxweiler et al. (2), found no significant association between dpm exposure and mortality due to lung cancer (or any other cause).

Thus, the strongest conclusion that can be drawn from these six studies is that the miners in the studies had an increased risk of lung cancer. These studies cannot relate such increased to any particular industrial exposure, lifestyle or combination of such factors. They provide no basis to attribute any specific adverse health effects in miners to dpm exposure.

Health Effects Institute Report

This past June, the Health Effects Institute (HEI) published a special report on the adequacy of published data for conducting quantitative risk assessments (QRA) on dpm and lung cancer (8). Included in the charge to the authors of the report, the HEI Diesel Epidemiology Expert Panel was to review "epidemiological data that form the basis of current quantitative risk assessments for diesel exhaust [and] identify data gaps and sources of uncertainty". A preliminary report was presented at a large public conference held earlier this year and the final report was peer-reviewed by a large number of scientists including contributors to, peer-reviewers of, and research cited in the MSHA Proposed Rules.

There is significant relevance of this HEI report to the MSHA Proposed Rules. If there are not adequate or appropriate data to perform a meaningful and rigorous QRA for dpm and lung cancer, then it is not scientifically appropriate or meaningful for MSHA to cite risk assessments to justify its proposed regulations. My earlier comments expressed my concerns that the published MSHA risk assessment was not scientifically correct or appropriate.

The HEI Panel first examined "published epidemiologic studies of diesel exhaust emissions and lung cancer" in order to determine whether any were of potential value for use in QRA. The Panel concluded that:

> "Only two such studies reported any quantitative exposure data associated in some manner with the occupational epidemiologic studies."

Neither of those two studies addressed concerns about miners. One was a study of railroad workers (e.g., Garshick et al. (9,10) discussed in my earlier comments. The other, a study of Teamsters by Steenland et al. (11,12), was not fully considered in the MSHA Proposed Rules because an important component (12) was published only late last year.

Thus in effect, the first conclusion of the HEI Panel was that there are no epidemiological studies of miners that reported any quantitative exposure data and none are suitable to support QRA on dpm and lung cancer. That conclusion affirms the discussion above regarding the epidemiological studies cited by Jon Kogut.

The Panel then further evaluated the railroad workers and Teamsters studies. With regards to the railroad workers, the Panel concluded that:

> "the railroad worker cohort study has very limited utility for QRA of lifetime lung cancer risk ... the Panel recommends against using the current railroad worker data as the basis for QRA in ambient settings".

The Panel's concerns, which apply equally to QRA for non-ambient occupational settings, are in sharp contrast to the statements contained in the MSHA Proposed Rules that describe the railroad workers studies as "the two most comprehensive, complete, and well-controlled studies available".

With regard to the Teamsters study, the Panel concluded that the study:

> "may provide reasonable estimates of worker exposures to diesel exhaust, but significant further evaluation and development are needed."

Summary

The Report of the HEI Panel confirmed that there are no epidemiological studies on miners that contain quantitative data on dpm exposure. It also raises serious doubts about the scientific meaning of quantitative risk assessments on exposure to dpm and lung cancer that are based on presently published data.

These findings are consistent with and lend significant support to my earlier comments on the MSHA Proposed Rules.

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Appendix C:

Comments of 11/05/01 by Jonathan Borak, MD and submitted to Hon. David Lauriski on behalf of the MARG Diesel Coalition

Diesel Particulate Matter Exposure of Underground Metal and Nonmetal Miners: Final Rule

Federal Register 66:5706-5910, 2001

Comments of Jonathan Borak, MD

1 The MSHA Statistical Analysis

MSHA embraces two nontraditional approaches to the interpretation and analysis of data from studies on dpm and cancer that obscure, rather than clarify the data upon which the MSHA risk assessment relies. One involves the apparent rejection of the standard approach to testing for statistical significance, while the other defines even very small amounts of increased risk as evidence of "clearly significant health hazard" [p.5785].

In embracing these two approaches MSHA ignores standard teaching (referred to by MSHA as "common convention" [p.5785]) about scientific inference, rejects generally accepted legal standards relied upon by the Federal judiciary and misrepresents key elements of the literature upon which these novel approaches rely.

Tests of Statistical Significance

The first of these involves the MSHA definition of "statistical significance" and the approach taken by MSHA to test for statistical significance and to interpret research findings. MSHA defines the concept of "statistical significance" in a standard, acceptable manner, but in practice the Agency ignores and violates that definition:

> "A 'statistically significant' finding is a finding unlikely to have arisen by chance in the particular group, or statistical sample, of persons being studied. An association arising by chance would have no predictive value for exposed workers outside the sample." [p. 5785] (emphasis added)

The Agency also presents a standard (albeit simplistic) explanation of why individual studies might not achieve statistical significance: 1) There may be no real difference; 2) The design of the study may not be adequate to demonstrate a difference (referred to as a lack of "power"). That explanation concludes:

> "lack of statistical significance in an individual study does not demonstrate that the results of that study were due merely to chance – only that the study (viewed in isolation) is statistically inconclusive." [p. 5785]

Because a study's statistical power can be determined, studies that lack statistical significance can be divided into two groups: those with sufficient power (i.e., negative studies), and those lacking sufficient power (i.e., "statistically inconclusive" studies).

Accordingly, it would have been expected that the MSHA analysis would divide the "47 known epidemiologic studies that MSHA considers relevant" into three groups: 1) positive studies (i.e., statistically significant positive studies); 2) negative studies (i.e., those lacking statistical significance but with sufficient power); and, 3) inconclusive studies (i.e., those lacking both statistical significance and power).

But such expectations are not met. Instead, MSHA finds 41 studies to be positive (i.e., show a positive relationship between exposure and cancer), and the other 6 to be negative (i.e., do not show such a positive relationship). Not one study is categorized as inconclusive. This results because MSHA ignored its own definitions:

> "Some degree of association between occupational dpm exposure and an excess prevalence of lung cancer was reported in 41 of the 47 studies... MSHA refers to these 41 studies as 'positive'. The 22 positive cohort studies are identified as those reporting a relative risk (RR) or standardized mortality ratio (SMR) exceeding 1.0. The 19 positive case-control studies are identified as those reporting an RR or odds ration (OR) exceeding 1.0. A study does not need to be statistically significant (at the 0.05 level) or meet all criteria described in order to be considered a 'positive' study." [p. 5775] (emphasis added)

Thus, MSHA created a category of "positive" studies category that did not require statistical significance, did not consider statistical power, and included studies that "have no predictive value for exposed workers outside of the sample" [p. 5785].

By contrast, the MSHA "negative study" category required both statistical significance and statistical power:

> "On the other hand, a study must meet two requirements in order to provide statistically significant evidence of no positive relationship: (1) the upper limit of its 95-percent confidence interval must not exceed 1.0 by an appreciable amount and (2) it must have allowed for sufficient exposure, latency, and follow up time to have detected an existing relationship." [p. 5785]

A naïve reader might assume the MSHA approach reflects efforts to be "precautionary", but more thoughtful examination reveals that the MSHA approach reflects fundamental misunderstandings (or misapplications) of standard methods of statistical inference. That fundamental error is revealed by considering the MSHA definitions of "positive" and "negative" in light of standard teachings ("common conventions" [p.5785]) of statistical analysis.

In most statistical analyses used to evaluate data of the sort considered here, the analyst first tests a "null hypothesis" which states that there is no difference between exposed and unexposed groups (or cases vs. controls) and that observed differences are due to chance alone. The goal of the analysis is to determine whether the observed data "refute the null hypothesis":

> "Most epidemiologic research is designed to evaluate scientific hypotheses. These hypotheses are often posed as qualitative propositions; the 'null' form of such propositions are specific statements, such as 'Eating small amounts of aluminum, compared with eating no aluminum, does not increase the rate of occurrence of Alzheimer's disease. ('Null' here implies that there is no relation between the postulated cause and effect, as in 'null hypothesis'). Stated in the null form, these specific propositions are, in principle, highly refutable." [KJ Rothman, S F Greenland *Modern Epidemiology* (2nd Ed). Philadelphia: Lippincott-Raven, 1998]

If the null hypothesis is "refuted", then the analysis indicates that a statistically significant difference exists between the groups and some "alternative hypothesis" is more likely than the null hypothesis. On the other hand, if the null hypothesis is not refuted, then the analytical conclusion is that the two groups are not significantly different and the analysis provides no support for the proposal that the exposure was causal. (It also provides no support for the opposite view, e.g., that exposure was protective).

If significant differences do exist and the null hypothesis is refuted, then it is necessary to determine whether the exposure increased the target events in the exposed group (e.g., exposure caused cancer) or prevented the target events in the exposed group (e.g., exposure prevented cancer). Either of those two alternative hypotheses could explain rejection of the null hypothesis, and either or both alternative hypotheses (i.e., causation or prevention) can be considered in the second step of the analysis.

(It should be noted that in many cases the correct alternative hypothesis is obvious from looking at the data, while in many others only one of the alternative hypotheses is operationally relevant. For example, in considering the effect of occupational exposure to dpm and lung cancer, the relevant alternative hypothesis is that exposure caused cancer; there is little practical relevance to testing whether the exposure was protective).

But MSHA does not follow that standard approach, which would have started with the null hypothesis: "Occupational exposure to dpm, as compared with no occupational exposure to dpm, does not increase the rate of lung cancer". From that starting point, MSHA would have divided the studies into two groups: 1) positive studies refuting the null hypothesis (i.e., studies with statistically significant increased rates of cancer); and 2) negative studies which do not refute the null hypothesis (i.e., studies lacking statistically significant increased rates of cancer).

The actual MSHA definitions of those terms, however, are not consistent with that standard approach. To the contrary, the MSHA definitions of "positive" and "negative" are not consistent with testing of the null hypothesis. Instead, they are consistent with a test of the alternative hypothesis: "Occupational exposure to dpm, as compared with no occupational exposure to dpm, decreases the rate of lung cancer". In other words, MSHA defined positive and negative as though the question to be answered was whether dpm was protective against lung cancer.

Thus, MSHA divided the "47 known epidemiologic studies" into two groups:

- 6 of 47 studies that provided statistical evidence that dpm exposure was protective against lung cancer

- 41 of 47 studies that do not provide statistical evidence that dpm exposure was protective against lung cancer

This situation arises because MSHA approached the analysis as though any study failing to document a protective effect of diesel must *perforce* be evidence of a harmful effect. That approach is wrong: The concern is not whether dpm fails to prevent cancer, but whether it causes that disease, and the absence of protection is not an indication of the potential to harm.

Relative Risks < 2.0

MSHA assembled a group of 41 epidemiological studies that are described as "positive" without regard to their statistical significance. Among those were numerous studies in which the observed differences between exposed and unexposed (or cases vs. controls) are very small. More specifically, the Agency indicates that a difference as small as 10 percent is an important and meaningful difference as a matter of policy:

> "It is important to note that MSHA regards a real10-percent increase in the risk of lung cancer (i.e., a relative risk of 1.1) as constituting a clearly significant health hazard" [p.5785].

That statement, at first seemingly straightforward, is so flawed as to be almost meaningless.

MSHA says that a "real 10-percent increase" is "clearly significant", but the concept "real increase" is not defined and no criteria are provided to determine when an increase is "real". From the MSHA arguments discussed earlier, it is clear that "real" is not synonymous with "statistically significant" (because statistical significance is not required) nor does it appear to be based on any other statistical analyses. Thus it seems that the criterion "real 10-percent increase" is actually undefined and subjective.

Accordingly, the MSHA criterion quoted above can be paraphrased as follows:

> It is important to note that MSHA regards a reported 10-percent increase in the risk of lung cancer (i.e., a relative risk of 1,1) without respect to its statistical significance or other tests of accuracy and/or validity as constituting a clearly significant health hazard.

Also troublesome is the MSHA policy decision to accept relative risks of 1.1 as defining the threshold for "significant health hazard". As a general rule, the Federal Courts have held that relative risks of less than 2.0 are not sufficient for showing causation [see discussion at p. 5787], but MSHA has rejected that view. Instead, MSHA argues that there is "ample precedent for utilizing epidemiologic studies reporting relative risks less than 2.0 in making clinical and public policy decisions" [p. 5787]. To justify its approach, the Agency cites two precedents, analyses of lung cancer risks due to cigarette smoking and indoor radon. Two references are cited, the 1989 *Report of the Surgeon General: Reducing the Health Consequences of Smoking* and the 1999 National Research Council (NRC) BEIR VI: *Health Effects of Exposure to Radon*. It is useful here to consider those two reports and why they may not be supportive of the approach taken by MSHA.

The reason that small increases of relative risks are viewed suspiciously is that they may reflect confounding or bias, rather than "true" biological effects. This concern is illustrated by the following statement found in that NRC Report :

> "A small relative risk implies that mean exposures of cases and controls differ by only a small amount, thus limiting study power. The detection of an excess risk of lung cancer is potentially complicated also by an inability to control completely for other lung-cancer risk factors, particularly cigarette-smoking, which has a relative risk of 10-20." [NRC BEIR VI: *Health Effects of Exposure to Radon*. Washington, DC: National Academy Press, 1999, at 379-30].

In such situations, large numbers of subjects are required to ensure that the differences observed are significant and meaningful. This is again illustrated by reference to the NRC Report on radon, which specifically addresses the concerns related to case-control studies demonstrating very small relative risks (e.g., 1.1-1.3):

> "this implies that the distribution of exposures for cases is very similar to the distribution of exposures for controls. As a consequence, substantial numbers of subjects are needed to establish a significant difference in the distributions and to estimate effects precisely." [NRC, *op. cit.* at 422-423]

Accordingly, it is interesting to review the actual references cited by MSHA, and to evaluate how size of samples differed between the dpm studies and those to which the Agency looks for support.

First, MSHA presents a table summarizing some of the data from Table 1 of the Surgeon General's 1989 *Report*. The data, derived from eight prospective epidemiological studies, describe relative risks of death from cardiovascular disease in smokers. We have obtained and reviewed all but one (a Japanese language study) and determined that those seven studies described mortality rates in more than a million people and considered nearly 10 million person-years of observation. Eight of the ten relative risk rates found in the table as reproduced by MSHA were in the range of 1.6-2.08 and all achieved statistical significance. It is difficult to see how such findings from huge, carefully performed studies lend support to the MSHA approach in interpreting the results of smaller, less controlled studies of which many did not achieve statistical significance.

Then MSHA refers to the eight largest residential epidemiological studies of radon exposure and lung cancer, as reanalyzed in a meta-analysis summarized by the NRC. In citing those studies, MSHA ignores that the residential studies were undertaken only after a causal relationship had been shown (by means of traditional statistical analyses) between higher exposures to radon and lung cancer in miners. Thus, the residential studies were analyzed to determine whether they were consistent with extrapolations derived from the experience of miners. In the case of diesel exhaust, there is no such certain relation to serve as an analytical benchmark.

Moreover, MSHA has elected to ignore the following NRC cautions and caveats

First, NRC determined that only studies with direct measurement of exposure should be considered:

> "The committee concludes that only analytic case-control studies that rely on direct measurement of radon in houses are useful for evaluating the risk of lung cancer posed by indoor-radon exposure." [NRC, *op. cit.* at 356-357]

This of enormous importance to the dpm measures because, as pointed out by the Health Effects Institute {17131} and others, there are few if any studies with direct dpm measurements. (This is discussed below with respect to two recent studies deemed by MSHA to be "highest rank"). Thus an approach consistent with NRC (and HEI) would find that there were almost no studies suitable for quantitative analysis of the risks of dpm and lung cancer.

Second, NRC reviewed a study in which three of the eight radon studies were "pooled" and reanalyzed:

> "The combined exposure-response relationship showed no trend with a pooled relative risk estimate of 1.0 with 95% CI (0.8-1.3)... Results suggest that relative risks were consistent with no effect of exposure..." [NRC, *op. cit.* at 416]

Third, a series of NRC-sponsored analyses and subgroup analyses of these studies led to ample cautionary warnings:

> "Comparisons of [redacted] analyses provide an additional framework for evaluating consistency among studies. Variations of risk patterns within subgroups and inconsistencies between studies compel a cautious interpretation of results. Three studies found no association with exposure overall and after intense subgroup analysis. Results of the other studies offer mixed support for a positive association." [NRC, *op. cit.* at 413]

Finally, these are NRC comments about the meta-analysis that MSHA has cited

> "In summary, there was a significant exposure-response relationship in the meta-analysis… However, meta-analyses are known to have numerous limitations, including an inability to explore adequately the consistency of results within and between studies and to control for potentially important confounding factors." [NRC, *op. cit.* at 421-422]

Accordingly, it is difficult to understand why MSHA views reports from NRC and the Surgeon General as supportive to its non-traditional approach to data analysis. To the contrary, both lend support to the view that the MSHA approach is irregular and, perhaps, irresponsible.

Methodological Weakness of the Studies

Discussed above is the concern that small relative risks can result from confounding and bias, and that such confounding are least likely to play an important role in well-designed studies with large numbers of subjects. Those methodological concerns contribute to the attribute that MSHA refers to as "power". Presumably, MSHA regards the dpm studies has having sufficient "power" to justify adopting very small increased relative risks as significant.

This is surprising in light of the manner in which MSHA described this literature in its 1998 Proposed Rule (1):

> "[N]one of the existing human studies is perfect and many contain major deficiencies… Shortcomings identified in both positive and negative studies include: possible misclassification with respect to exposure; incomplete or questionable characterization of the exposed population; unknown or uncertain quantification of diesel exhaust exposure; incomplete, uncertain, or unavailable history of exposure to tobacco smoke and other carcinogens; and insufficient sample size, dpm exposure, or latency period. [MSHA: Diesel Particulate Matter Exposure of Underground Metal and Nonmetal Miners: Proposed Rule. *Fed Reg* 63:7532]

Accordingly, it seems even more difficult to understand the MSHA justification for reliance upon such small increased relative risks to justify their Final Rule. One example of such justification is the Agency's reliance on the "Healthy Worker Effect" to

explain the finding or small or no differences in various studies. As described below, such reliance is without theoretical or practical support.

Healthy Worker Effect

The MSHA Final Rule refers thirty-eight times to the "Healthy Worker Effect" (HWE), a form of epidemiologic bias that MSHA describes as follows:

> "Because workers tend to be healthier than non-workers, the prevalence of disease found among workers exposed to a toxic substance may be lower than the rate prevailing in the general population, but higher than the rate occurring in an unexposed population of similar workers. This phenomenon is called the "healthy worker effect" [p. 5784].

As discussed in the Final Rule, the MSHA position is that HWE reduces observed rates of lung cancer in dpm-exposed workers, thereby tending to conceal or minimize the apparent adverse effects of exposure. As a result of HWE, MSHA argues, some dpm studies fail to show an increase in lung cancer mortality (or show lower than expected rates of cancer), while others demonstrate only insignificant increases. If the HWE were considered, the MSHA argument continues, then most of these studies would have found more positive carcinogenic effects. Therefore, the absence of an effect in specific studies reflects study bias (i.e., HWE), not the absence of biological potency for dpm.

For example:

> "...factors that would tend to obscure or deflate an excess risk of lung cancer, if it existed: (1) a healthy worker effect..." [p. 5790].

> "...several commenters cited this study as evidence that exposure to diesel emissions was not causally associated with an increased risk of lung cancer ... These commenters apparently ignored the investigators' explanation that the low SMRs they reported were likely due to a healthy worker effect" [p.5792].

> "...the healthy worker effect can influence results even when the age-adjusted mortality or morbidity rate observed among exposed workers is greater than that found in the general population. In such studies, comparison with the general population tends to reduce the excess risk attributable to the substance being investigated" [p. 5784].

MSHA also discusses adjustments that can be made to overcome HWE and points to a method used by Bhatia et al (2) who arithmetically adjusted standardized mortality rates for lung cancer in dpm-exposed workers:

> "We recalculated the SMR for all causes of death after removing observed and expected cases of lung cancer. Then, we adjusted the expected number of lung cancer deaths by multiplying the general population expected number of the

> SMR for all causes excluding lung cancer". {Bhatia R, et al.: Diesel exhaust exposure and lung cancer. *Epidemiology* 9:84-91, 1998]

An assumption that is implicit throughout the MSHA discussion, and explicit in the approach of Bhatia, is that the effects of HWE on observed lung cancer mortality are essentially equivalent (i.e., proportional) to its effects on mortality from all causes. But there are reasons to argue that this is not correct. In fact, there are reasons to argue that HWE is not even relevant to lung cancer. As discussed below, that latter view is shared by a large number of prominent epidemiologists.

HWE is generally attributed to selection bias and confounding {17072}(3,4). With respect to selection bias, HWE results when there is selective workforce inclusion of healthier persons and selective exclusion of less healthy persons. This first occurs at the time of hire (when healthy individuals are selected) and it can also occur later, if workers who become unhealthy are dismissed or voluntarily withdraw from the workforce. If less healthy people are excluded from study cohorts (both those initially excluded and others who are later excluded), then those cohorts will necessarily be "healthier" specifically because the unhealthy have been removed from consideration.

Confounding can contribute to HWE in several ways. It occurs when there are advantages of employment that influence workers' health status for reasons unrelated to the nature or risks of the work. For example, if workers have access to better health care than that available to the unemployed and if better health care leads to better health, then working people will be healthier than the unemployed. Another example stems from differences in socio-economic status (SES) between employed and unemployed people: because SES is an important predictor of health status, employed people with higher SES will be healthier than the lower SES unemployed without regard to the types of work that lead to higher SES.

Most epidemiologists agree that the effects of selection bias are generally more important early in a person's work life and do not apply equally to all diseases and disease processes. For example, the advantage that stems from the initial selection of healthy individuals declines over tim

> "When follow-up is achieved for a total cohort, including those that quit or retire early for health reasons, then the initial HWE associated with active employment declines with time, because of the absence of any continued selection process." [McMichael AJ: Standardized mortality ratios and the "healthy worker effect": Scratching beneath the surface. *J Occup Med* 18:165-168, 1976].

> "The mortality of employed persons, relative to the general population, is lowest during the period immediately after starting employment. Fox and Collier (5) found that the all-causes mortality of men within five years of entering the industry was as low as 37% of that expected... The effect decreased with length of time since entry into the cohort and had almost disappeared after 15 years... Many other studies have also found relatively low relative risk for the early years

> of follow-up, with relative risks slowly approaching 1.0 as follow-up continued." [Checkoway H et al.: *Research Methods in Occupational Epidemiology*. New York: Oxford University Press, 1989].

Also, some diseases are more likely to be identified during initial screening of job candidates. For example, persons with obvious physical deformities, symptomatic respiratory and bowel diseases, and congenital cardiac malformations are more likely to be identified and excluded during pre-employment exams:

> "During the first 15 years of follow-up, the lowest relative risks are seen for nonmalignant respiratory and digestive diseases. Although these are not common causes of death, potentially fatal diseases such as asthma and colitis are manifest by age 20 and are a factor in employment." [Monson RR: Observations on the healthy worker effect. *J Occup Med* 28:425-433,1985]

> "Incapacitating diseases that would keep individual from working would be observed very infrequently among employed populations. Very few workers with tuberculosis work in steel mills." [Sterling, TD, Weinkam, JJ: Extent, persistence, and constancy of the healthy worker or healthy person effect by all and selected causes of death. *J Occup Med* 28:348-353, 1985]

By contrast, diseases such as cancer are less amenable to early identification. Few young workers can be identified as being at increased risks for cancer. It is especially unlikely that pre-employment exams will identify and exclude those individuals who will develop cancers following long latency periods, e.g. after 15-20 years or longer. For example, consider the following statement from Richard Doll as quoted in (4):

> "It is extremely difficult to predict who will get cancer (apart from knowledge of the individual's smoking habits) and, unless there is selection against smokers, it is not evident that any of the factors... [leading to HWE]... will have any material effect on the risk of cancer after (at the most) 5 years" (4).

More compelling is the following composite of statements by ten of the world's leading epidemiologists (Sir Richard Doll, Phillip Enterline, Geoffrey Howe, AJ McMichael, Olli Miettinen, Richard Monson, William Nicholson, TD Sterling, and JJ Weinkam) that were submitted to the Workers' Compensation Board (WCB) of Ontario and later compiled and published (4):

> "The HWE is likely to be small in: 1) 'diseases unlikely to be manifest at time of employment' (Enterline) or diseases that 'occur late in life' (Enterline), or in other words, diseases of 'old age' that are less related to health status at start of employment than are diseases of young age (Monson), e.g., cancer; 2) diseases with symptoms that 'appear only a few years before death occurs' (Enterline), or diseases that have a 'high fatality rate' which makes initial selection bias disappear more rapidly than other long term chronic diseases (Howe), or diseases that 'have a typically silent course until their later stages' (McMichael),

> e.g., cancer, particularly lung cancer; and 3) diseases whose risk factors have not been 'addressed in the selection processes by which individuals enter and remain in the workforce' (McMichael), e.g., cancer " (4).

In short, a substantial proportion of the epidemiologists surveyed agreed that HWE is not uniform over the work life of individuals and does not pertain equally to all diseases and disease processes. Contributors to the WCB survey proposed that:

> "causes of death, in the order of decreasing effect on the HWE, are: nonmalignant diseases of respiratory, digestive, endocrine and urinary systems; cardiovascular diseases, circulatory diseases, and ischemic heart diseases; all causes; cancers other than lung; all cancers; lung cancer" (4).

> "Most contributors said that the HWE is unlikely and, therefore, can be ignored in cancer studies" (4).

Moreover, most of those epidemiologists did not support the concept of adjusting or correcting results as suggested by MSHA:

> "Sterling and Weinkam suggested that 'some corrections for HWE are possible' ... Many other contributors, however, do not accept a single correction factor for the HWE. They thought that since a number of factors modify the HWE, it is not possible to make generalizations about a single HWE, and, therefore, the suggestion of correcting for such an effect using a single figure would not be valid" (4).

In summary, there is little support in the epidemiology community for the approach taken by MSHA with respect to HWE in this dpm-related context. MSHA has neither critically reviewed the epidemiologic literature nor defended its reliance on HWE as a means by which it refutes those findings that disagree with its regulatory objectives.

MSHA has ignored the general view that studies of cancer, particularly lung cancers, are not much affected by HWE. MSHA has also proposed correction and adjustment methods that assume uniformity of the HWE, an approach that directly conflicts with the views of many of the epidemiologists cited above.

As a result, MSHA has biased its own evaluation of this literature in a manner that exaggerates the alleged human cancer risks of dpm, while diminishing studies that are not directly supportive of the MSHA perspective.

2. Two New "Highest Rank" Studies

As means of rebutting criticism of its Proposed Rule, the MSHA Final Rule embraces two recent studies, one by Saverin et al (6) and the other by Johnston et al (7) that are described as the "highest rank" because they met MSHA criteria for quality of exposure assessment.

> "MSHA agrees that the quality of exposure assessment affects the value of a study for even hazard identification. Accordingly, MSHA has divided the 47 studies into four categories, depending on the degree to which exposures were quantified for the specific workers included. This ranking refers only to the exposure assessment and does not necessarily correspond to the overall weight MSHA places on any of the studies.
>
> "The highest rank, with respect to this criterion, is reserved for studies having quantitative, concurrent exposure measurements for specific workers or for specific jobs coupled with detailed work histories. Only two studies (Johnston et al and Saverin et al) fall into this category". [p. 5784].

This is reiterated when MSHA responded to criticisms of its methods:

> "Furthermore, two of the studies now available ... utilize essentially concurrent exposure measurements, and both show a positive association (Johnston et al and Saverin et al)" [p. 5808].

Other statements also indicate the special importance that MSHA gave to these two studies. For example, they were listed among eight studies described as providing "the best currently available epidemiologic evidence relating dpm exposure to an increased risk of lung cancer... this select group" [p. 5795]. Also, with reference to three studies (Johnston et al and Saverin et al were two of those three) MSHA stated that it placed "considerable weight on the fact" the studies were timely and found a positive effect: "the most recent epidemiologic studies available – reported an association between diesel exposure and an increased risk of lung cancer" [p. 5792].

Moreover, it seems that these two studies were important to MSHA as a means of deflecting criticism that Dr. Peter Valberg and I independently submitted in response to the MSHA Proposed Rule:

> "Moreover, two newer studies pertaining specifically to miners do contain dpm exposure assessments based on concurrent exposure measurements (Johnson et al; Saverin et al). The major limitations pointed out by Drs. Valberg and Borak with respect to other studies involving miners do not apply to these two studies" [p. 5790].

Thus, in light of the significance that MSHA has placed on the Saverin and Johnston studies, it is useful to examine them more closely.

The Saverin Study

This reexamination of the Saverin study considers two specific issues: 1). Were exposure measurements "concurrent"? 2). Did the Saverin study find positive associations? These issues are discussed below.

Were exposure measurements "concurrent"?

The Saverin et al study (6) measured dpm exposure in a German potash mine during 1992:

> "In 1992, measurements of the concentration of total carbon i.e., elemental and organic carbon in total, in the airborne fine dust fraction were performed... With personal dust sampling, and area dust sampling where suitable, a set of 255 concentration values covering all workplaces was obtained..." [Saverin, p.416].
>
> "The mining technology and the type of machinery used did not change substantially after 1970. Therefore, the concentrations measured in 1992 were chosen to represent exposure throughout the study period" [Saverin, p.416].
>
> "Figure 1. Frequency distributions of 255 concentration measurements, performed in 1992" [Saverin, p.418].

But, according to Saverin et al, the mine had been shut down in 1991 and most of the workers had then been discharged:

> "During 1969 to 1970, the potash mines in the South Harz Mountains area of Germany changed technology to the use of mobile diesel powered vehicles. From that time until the mines were closed in 1991, the underground workforce was exposed to diesel exhaust" [Saverin, p.416] (emphasis added)
>
> ""When the mines cased production in 1991, most of the miners were dismissed and abandoned underground work and exposure" [Saverin, p.418] (emphasis added).

It seems, therefore, that the Saverin exposure survey was conducted after the mine had ceased production and after most miners had been dismissed. No details are provided regarding how and when the closed mine was reopened, how and when nearly one thousand workers were rehired, or how and when mothballed and scrapped mining equipment was restored to operability. Given the likely high costs of returning a closed mine to full operation, plus the fact that the East German potash mining industry "was sparsely financed" [p. 420], it would be surprising if this mine was returned to production solely for this study. Instead, it is more probable that exposures were measured during a staged simulation, not during routine mining operations.

Accordingly, it seems that Saverin et al and MSHA have both offered an inappropriate argument to justify their fundamental assumption that exposures measurements made in 1992 were representative of exposures from 1970 to 1991:

> "the mining technology and the type of machinery used did not change substantially after 1970. Therefore, the concentrations measured in 1992 were

> chosen to represent exposure throughout the study period" [Saverin et al, p.416, MSHA p.5793].

The appropriate concern was whether the study considered appropriate and typical mining conditions and operations, not whether "mining technology and the type of machinery" had changed. If the mine was not operating in a manner similar to its historical routine, then the exposure measurements were not representative of "exposure throughout the study period" and the issues of technology and machinery type are of no particular relevance.

On the basis of the information provided in Saverin et al, it seems likely that exposures were measured during a staged simulation, not during routine mining operations. On that basis, we disagree with the MSHA characterization of this study. It seems that the exposure assessment was probably not concurrent with operations and did not reflect the mine conditions during its historical operations.

The fact that the exposure assessment was conducted after mine production had ceased has other important implications for the MSHA risk assessment. If the mine was not at full operation during the Saverin exposure assessment, then the dpm levels probably underestimated the levels that would have been found during full operation. Risk calculations derived from such exposure assessments would necessarily overestimate the risk associated with dpm exposure. Any risk estimates extrapolated from these data would be thereby biased so as to overestimate the putative carcinogenic potency of dpm.

Did the Saverin study find positive associations?

The results of the Saverin study do not achieve statistical significance and are ambiguous. Even when the data were subjected to various transformations and evaluated by a variety of statistical tests using non-standard ultra-liberal criteria for determining significance, no significant effects of exposure could be found:

> "The internal sub-cohort comparison on the workshop and the production group indicated an insignificantly elevated lung cancer risk. The risk estimate was based on only 17 deaths from lung cancer and so was susceptible to misdiagnosis and random imbalance in smoking habit not covered by the confidence interval. Cox regression analysis utilizing the individual cumulative exposures produced a similar result, the Poisson regression estimates being somewhat smaller... The principal finding of the study ... was not statistically significant even at a 90% level" [Saverin, p. 421] (emphasis added)

MSHA apparently agrees with that conclusion:

> "This study has two important limitations that weaken the evidence it presents of a positive correlation ... a significant probability that a correlation of the

> magnitude found could have arisen simply by chance, given that it were based on a relatively small number of lung cancer cases" [MSHA, p.5794].

Moreover, it is necessary to realize that the study data are also consistent with an alternative interpretation of the data, which argues that dpm is actually protective! The potash miners had a lower risk of lung cancer than that expected in the East German population (SMR = 0.78). That is surprising because all of the workers were exposed to dpm and 64-70% of them were smokers, a rate that Saverin notes to be "higher than in the general population". Saverin et al and MSHA explain the finding of an SMR < 1.0 by invoking the healthy worker effect. But, as discussed above, most epidemiologists regard the health worker effect as having little or no importance for studies of lung cancer. In fact, even Saverin et al indicates that one should be cautious in attributing their results to such effects:

> "lung cancer mortality, too, may be subject to health-worker selection and is probably also subject to an increasing trend over time, paralleling the cumulating exposure. If so, this could spuriously enhance an effect of exposure" [Saverin, p.421].

Thus, the Saverin et al. data are also consistent with the hypothesis that exposure to dpm decreases the lung cancer risks of cigarette smoking. (It is not my objective to advance this particular thesis, only to point out the weaknesses and inconsistencies inherent to the Saverin et al data and the failure of MSHA to thoughtfully evaluate the study).

The Johnston Study

Reexamination of the Johnston study considers similar issues: 1). Did the study measure diesel emissions and were the measurements concurrent? 2). Did the study adequately control for confounding?

Was diesel measured? Were measurements concurrent?

The Johnston et al study (7) considered exposure to diesel emissions in six mines, but it did not directly measure those emissions in any of the mines. Instead, the study estimated dpm exposures by two indirect methods. In one method, dpm was estimated from total respirable dust levels that were then adjusted using a series of other estimated values. For example, consider the Johnston et al "Short summary" of the "estimation of respirable diesel exhaust particulate exposures" from dust exposure measurements for "locomotives operating downstream (in terms of the ventilation air) of the workplace" [Johnston, p. 21]:

> "Where the locomotives operated downstream of the face areas ... the diesel exhaust particulate exposure concentrations for the locomotive drivers are estimated as the measured total-respirable dust concentration minus the

> measured ash content, minus the estimated concentration of any other non-diesel combustible-respirable material (mainly coal dust).
>
> "The respirable coal dust concentration is estimated by comparison of the quartz content for drivers with the average for face workers, on the assumption that the ratio of respirable coal dust to respirable quartz is the same for both... Exposure of men operating at workplaces upstream of the locomotive to diesel exhaust particulate is assumed to have occurred only during travel. It is also assumed that all travelers, including the drivers, were exposed to the same instantaneous diesel particulate concentrations during travel" [Johnston, p. 21-22]. (emphasis added)

It can be seen that this approach did not reflect "concurrent measurements" of dpm, but calculated estimates derived from a prior series of estimates and assumptions.

Similarly, dpm exposures were estimated indirectly from prior measures of nitrogen oxides:

> "A second (largely) independent mechanism for estimation of the respirable diesel exhaust particulate exposure concentrations for the same groups of workers is ... based on existing measurements of the concentrations of oxides of nitrogen to which these groups of workers were exposed, and on estimates of the proportion of this that arose from the exhaust of the diesel locomotives. This estimate of the exposure concentration for diesel-exhaust-derived NO_x is then divided by the estimated ratio of the concentration of oxides of nitrogen to that of respirable particulate in the exhaust emission, to convert to the latter.
>
> "In practice, the way that we have chosen to estimate this NO_x-to-particulate ratio is related to the measured dust concentrations reported in the PFR studies, but is largely (but not wholly) independent of the calculations used here to "convert" those to respirable diesel exhaust particulate exposure concentrations [Johnston, p. 21-22]. (emphasis added)

Thus, it is again clear that there were no "concurrent measurements" of dpm, but a series of indirect measurements converted to dpm estimates by means of a series of prior estimates and assumptions, several the same as used in the preceding method.

In light of the methods actually used by Johnston et al, we disagree with the MSHA description of this study as "highest rank" for the quality of its exposure assessment. In fact, it seems that MSHA itself agrees with our views of the limitations in this study:

> "Two limitations of this study weaken the evidence it presents... First, although the exposure assessment is quantitative and carefully done, it is indirect and depends heavily on assumptions linking surrogate measurements to dpm exposure levels" [MSHA, p. 5793].

Moreover, the two approaches that Johnston et al used by estimate dpm exposures yielded dissimilar results. In the Final Rule, MSHA describes this in generous terms:

> "In four of the six dieselized mines, the NOx-based and dust-based estimates of dpm were in generally good agreement" [MSHA, p. 5792].

It is surprising that MSHA viewed those results as "generally good", because Johnston et al did not. With regards to the exposure estimates for locomotive drivers, the study authors concluded as follows:

> "The two separate estimates for Colliery Q, for Colliery W and for Colliery Y compare reasonably well. However, for Colliery K and for Colliery X, the estimated respirable diesel exhaust particulate exposure concentration from the NOx data is less that half of that derived from the PFR dust data in all cases. The largest differences occur for the Flockton seam at Colliery K, and for the Barnsley seam at Colliery X, where, in each case, the first of the estimates are approximately 6 times the last

> "Given the differences in measurement technique and the assumptions applied for both sets of estimates, the general finding is that the level of agreement between the two set is considered to be encouraging" [Johnston, p. 52].

In summary, we find that Johnston et al did not measure diesel and that the measurements were crude and imprecise. Accordingly, we believe that MSHA has mischaracterized the study methods and the qualities of its exposure assessment.

Did the study control for confounding?

In the Final Rule, MSHA states clearly that its valuation of studies gave important consideration to the important role of confounding. With respect to the criterion 'Composition of Comparison Groups', MSHA states:

> "MSHA includes bias due to confounding variables under this criterion if the groups differ systematically with respect to such factors as age or exposure to non-diesel carcinogens. For example, unless adequate adjustments are made, comparisons of underground miners to the general population may be systematically biased by the miners' greater exposure to radon gas" [p. 5783].

This concern is repeated several pages later in the Final Rule:

> "With respect to lung cancer, there are many reasons why workers from a particular group of mines might not be selected for study... many mines contain radioactive gases and/or respirable silica dust, making it difficult to isolate the effects of a potential carcinogen" {p. 5789].

Accordingly, is a surprise that in its evaluation of the Johnston study, MSHA described the presence of important confounding and recognized the study authors' concerns about that confounding, yet then disregarded its own criteria in an enthusiastic rush to embrace the Johnston study:

> " limitations of this study weaken the evidence it presents...the highest estimated cumulative dpm exposures were clustered at a single coal mine, where the SMR was elevated relative to the regional norm. Therefore, as the authors pointed out, this one mine greatly influences the results and is a possible confounder in the study. The investigators also noted that this mine was 'found to have generally the higher exposures to respirable quartz and low level radiation'. Nevertheless, MSHA regards it likely that the relatively high dpm exposures at this mine were responsible for at least some of the excess mortality. There is no apparent way, however, to ascertain just how much of the excess mortality (including lung cancer) ... should be attributed to high occupational dpm exposures and how much to confounding factors distinguishing it (and the employees working there) from other mines in the study" [MSHA, p. 5793].

Thus, it seems that MSHA simply decreed that confounding in Johnston et al was of insufficient importance to doubt the study and its conclusions. But the decision to ignore confounding at that mine ("Colliery Q") was significant for several reasons. First, the manner in which it was done suggests that MSHA did not understand the importance of that one mine to determining the study results.

In the Final Rule, MSHA says:

> "as the authors pointed out, this one mine greatly influences the results" [MSHA, 5793},

but that statement substantially understates its importance, as described in the report by Johnston et al:

> "The strength of the relationship between lung cancer mortality and lagged diesel exposure was <u>entirely dependent on the relatively high exposure at Colliery Q</u> where mortality was slightly higher than regional background rates" [Johnston, p.94] (emphasis added)

Moreover, to determine the influence of Colliery Q on the overall findings, Johnston et al repeated their analyses after excluding the men from pit Q:

> "With this reduced cohort, diesel exposure was <u>not even close to being statistically significant</u> and, in fact, resulted in estimated relative risks per unit exposure lower than 1.0 for the 15-year and 25-year lagged exposures" [Johnston, p. 89] (emphasis added)

Thus, the findings in this particular study, which MSHA described as among the "select group"... "the best currently available epidemiologic evidence relating dpm exposure to an increased risk of lung cancer" [MSHA, p. 5795], is entirely dependent on one of ten mines in which elevated levels of dpm, quartz and radon were all simultaneously present. As an act of faith, MSHA has determined that the excess risk of lung cancer in that mine was due to the dpm. In reaching that conclusion, MSHA violated its own key criteria for this literature review.

3. References

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Curriculum Vitae

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Courses Taught: 1997-Current

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Graduate-level course listed in the School of Medicine, Department of Epidemiology and Public Health.

2001-Current EHS 551a and b. Seminar in Environmental Health: Lecturer
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2002-Current EHS 510b. Fundamentals of Environmental Health and Risk Assessment: Lecturer
Graduate-level course listed in the School of Medicine, Department of Epidemiology and Public Health.

1997-Current EHS 575b/INT 151b. Introduction to Occupational and Environmental Medicine: Lecturer Graduate-level course listed in the School of Medicine, Department of Epidemiology and Public Health and the Department of Internal Medicine.

1999-2002 EHS 509a. Environmental Toxicology: Lecturer
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2000-2001 EHS 580a. Special Topics in Society and Risk Assessment: Course Director
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Thesis and Dissertation Committees

2002 Primary Advisor: Susan Chemerynski: "Methodological Uncertainties in the Exposure Assessment of Diesel Particulate Matter: Implications for Risk Assessment". Masters Thesis for MPH in Environmental Health Sciences, Yale School of Medicine

2003 Committee Member: Montira Pongisiri: "Institutional Capacity to Assess and Manage Risk-Tradeoffs: The DDT/Malaria Dilemma". Dissertation for PhD in Environmental Policy, Yale School of Forestry and Environmental Studies

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ORGANIZATIONAL ACTIVITIES

United States Environmental Protection Agency

1996-Current National Advisory Committee to Develop Acute Exposure Guideline Levels for Hazardous Substances (NAC/AEGL)

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American College of Occupational and Environmental Medicine

1999-2002 Board of Directors
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1993-Current Council on Scientific Affairs (Chairman 1999-Current)
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1993-1999 Course Director, Core Curriculum in Environmental Medicine.
1992-Current Committee on Environmental Medicine (Chairman 1993-96)

1993-2000 Committee on Medical Surveillance (Chairman 1998-2000)
1996-1998 Seminar Chairman, 1998 American Occupational Health Conference
1992-1993 Scientific Chairman, 1993 State-of-the-Arts Conference
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1995-Current Committee on Government Affairs
1992-1997 Committee for Liaison with Government Agencies
1995-1997 Committee on Distance Learning (Associate Chairman 1996-1997)
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American Industrial Hygiene Association
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1994-1996 Section of Preventive Medicine (Chairman 1994-96)
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Occupational and Environmental Medical Association of Connecticut
1992-1998 Board of Directors
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1992-1993 Secretary-Treasurer

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Connecticut College of Emergency Physicians
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1987-1992 Medical Advisory Committee on Blood Programs

Connecticut Dept of Health Services, Office of Emergency Medical Services
1985-1988 Helicopter Over-site Committee (Chairman, Patient Care Review)
1987-1988 Trauma Network Committee

Emergency Medical Systems Council of South Central Connecticut
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New Haven County Medical Association
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PUBLICATIONS and EDITORIAL ACTIVITIES

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1999-Current Editorial Board, American Industrial Hygiene Association Journal

1997-Current Associate Editor, OEM: Occupational and Environmental Medicine Report

1992-Current Editorial Reviewer: Annals of Emergency Medicine; Journal of Occupational and Environmental Medicine; Southern Medical Journal; Toxicology and Applied Pharmacology; Toxicology & Industrial Health; Inhalation Toxicology; Critical Reviews in Toxicology; Human and Ecological Risk Assessment Journal of the Air & Waste Management Association

1991-Current Editorial Board, OEM: Occupational and Environmental Medicine Report

1988-92 Peer Reviewer, Case Studies in Environmental Medicine, US Agency for Toxic Substances and Disease Registry, Atlanta, Georgia

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Borak J, Becker C, Ducatman AM, Kiper HM, McKinnon HW, McLellan RM, Mitchell FL, Russi M: "Core Curriculum in Environmental Medicine". (Continuing Education Program, accredited for 14 CME credits by American College of Occupational and Environmental Medicine and included as a component of the "Essentials of Occupational and Environmental Medicine").

State-of-the-Art Conference, American College of Occupational and Environmental Medicine, Dallas, 1993

American Occupational Health Conference, American College of Occupational and Environmental Medicine, Chicago, 1994

American Occupational Health Conference, American College of Occupational and Environmental Medicine, Las Vegas, 1995

American Occupational Health Conference, American College of Occupational and Environmental Medicine, San Antonio, 1996

American Occupational Health Conference, American College of Occupational and Environmental Medicine, Orlando, 1997

American Occupational Health Conference, American College of Occupational and Environmental Medicine, Boston, 1998

Borak J: "Hazardous Materials Training for Hospital Emergency Personnel" (16-Hour Continuing Education Program).

Occupational Safety & Health Spring Academy, Concord, NH. (Sponsored by Harvard School of Public Health), 1992.

Exeter, NH (Sponsored by Exeter Hospital), 1992.

Bentley College, Waltham, MA. (Sponsored by Harvard School of Public Health), 1992

Pittsburgh, PA (Sponsored by Allegheny County Health Department), 1994.

Bombay, India (Sponsored by US Agency for Industrial Development, World Environment Center and the National Safety Council of India), 1996

Vadadora, India (Sponsored by US Agency for Industrial Development and World Environment Center and the National Safety Council of India), 1996

Cochin, India (Sponsored by US Agency for Industrial Development, World Environment Center and the National Safety Council of India), 1996

Borak J: "An Introduction to Industrial Hazards for Physicians". (Continuing Education Program, accredited for 7 Category CME credits by American College of Emergency Physicians, 1988-92).

Wallingford, CT (Sponsored by Connecticut ACEP), 1988.

Bristol, PA (Sponsored by Rohm and Haas Company), 1988.

Pasadena Medical Center, Pasadena, TX (Sponsored by ARCO Chemical) 1988.

Newtown Square, PA (Sponsored by ARCO Chemical Company), 1989.

Hospital of St. Raphael, New Haven (Sponsored by Connecticut ACEP), 1989.

Rhode Island Hospital, Providence (Sponsored by Rhode Island ACEP), 1990.

Pre-Conference Seminar, Disaster '91: The International Disaster Management Conference; Orlando, 1991.

Seattle (Sponsored by Washington ACEP), 1991

Concord, MA (Sponsored by Emerson Hospital), 1991.

Concord, NH (Sponsored by Harvard School of Public Health), 1992.

Boston, MA, (Sponsored by Conference of Boston Teaching Hospitals), 1992

Pittsburgh, PA (Sponsored by Allegheny County Health Department), 1994.

Map Ta Phut, Thailand (Sponsored by US Agency for Industrial Development and World Environment Center), 1995

Bangpoo, Thailand (Sponsored by US Agency for Industrial Development and World Environment Center), 1995

Serang, Indonesia (Sponsored by US Agency for Industrial Development and World Environment Center), 1995

Boston, MA (Sponsored by Metropolitan Boston EMS Council), 1996.

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